

Hydrogel of Biodegradable Cellulose Derivatives. I. Radiation-Induced Crosslinking of CMC

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ABSTRACT: Radiation crosslinking of carboxymethylcellulose (CMC) with a degree of substitution (DS) from 0.7 to 2.2 was the subject of the current investigation. CMC was irradiated in solid-state and aqueous solutions at various irradiation doses. The DS and the concentration of the aqueous solution had a remarkable effect on the crosslinking of CMC. Irradiation of CMC, even with a high DS, 2.2 in solid state, and a low DS, 0.7 in 10% aqueous solution, resulted in degradation. However, it was found that irradiation of CMC with a relatively high DS, 1.32, led to crosslinking in a 5% aqueous solution, and 20% CMC gave the highest gel fraction. CMC with a DS of 2.2 induced higher crosslinking than that with a DS of 1.32 at lower doses with the same concentration. Hence, it was apparent that a high DS and a high concentration in an aqueous solution were favorable for high crosslinking of CMC. It is assumed that high radiation crosslinking of CMC was induced by the increased mobility of its molecules in water and by the formation of CMC radicals from the abstraction of H atoms from macromolecules in the intermediate products of water radiolysis. A preliminary biodegradation study confirmed that crosslinked CMC hydrogel can be digested by a cellulase enzyme.

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INTRODUCTION

Radiation is a very convenient tool for the modification of polymer materials through crosslinking, grafting, and degradation. Such modified materials can become useful products for daily life. For instance, foam and automobile tires are often produced by radiation crosslinking. Recently, it was demonstrated that radiation utilization is effective for environmental conservation. To reduce CS₂ and NaOH used in the production of viscose rayon, high-energy radiation was employed to decrease the molecular weight of cellulose.¹

After use, a biodegradable polymer is converted to CO₂ and H₂O by digestion and by bacterial degradation in the soil. This kind of polymer has been actively developed because it is environmentally friendly. We have reported that poly(ϵ -caprolactone) (PCL) radiation crosslinked in a supercooled state has high heat stability and at a low dose of irradiation (30 kGy) has improved processability.^{2,3} Biodegradation of crosslinked PCL is not affected by formed network structure.⁴

Hydrogels can be prepared from water-soluble polymers such as poly(vinyl alcohol), poly(ethylene oxide) (PEO), and poly(vinylpyrrolidone) by radiation crosslinking.⁵ Such hydrogels can accelerate the healing of wounds and therefore can be effectively used as a wound dressing.⁶ There have

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been reports on several studies on the synthesis of biodegradable hydrogels of poly(amino acids) such as poly(γ -glutamic acid)⁷ (PGA), poly(γ -lysine),⁸ and poly(aspartic acid)⁹ (PAsp) by radiation crosslinking in an aqueous solution for use in cosmetic, medical, and superabsorbent materials. Natural polymers such as alginate and carrageenan and cellulose derivatives can form hydrogels in the presence of metal ions.¹⁰ However, these polymers degrade upon irradiation.¹¹ This article reports on the results of radiation crosslinking of CMC with different degrees of substitution (DS) at various irradiation conditions.

EXPERIMENTAL

Materials

Carboxymethylcellulose (CMC) used in this experiment was a commercial product obtained from Daicel Co. Ltd., Japan. The DS of the CMC was from 0.71 to 2.2. The average molecular weight of the CMC was estimated by measuring intrinsic viscosity (Table I). All chemicals were analytical grade.

Sample Preparation and Irradiation

Deionized water was added to CMC, which was then mixed until homogeneous. For high concentrations, above 10%, the CMC was kneaded well with water by a glass bar. In the presence of air, irradiation of the mixture was carried out in a polyethylene bag; for air-free irradiation, the mixture was heat-sealed in a poly(vinylidene chloride) bag to make it impermeable to air, after removal of the air by a vacuum machine. Irradiation of the sample was done with gamma rays

generated from a ⁶⁰Co source at a dose rate of 10 kGy/h.

Gel Content and Swelling of Hydrogel

After irradiation, the CMC mixed with water was dried. Then the gel content in the dried CMC was estimated by measuring its insoluble part after immersion in deionized water for 48 h at room temperature. The gel fraction was calculated as follows

$$\text{Gel fraction (\%)} = (G_d/G_i) \times 100 \quad (1)$$

where G_i is the initial weight of dried CMC after irradiation and G_d is the weight of the insoluble part after extraction with water.

The swelling of crosslinked CMC was estimated according to Japan Industrial Standard (JIS) K8150. The dry gel was immersed in deionized water or an 0.9% NaCl aqueous solution for 24 h at room temperature. After swelling, the hydrogel was filtered by a stainless-steel net of 30 mesh. Swelling was calculated as follows

$$\text{Swelling} = (G_s - G_i)/G_i \quad (2)$$

where G_s is the weight of hydrogel in a swollen state.

Viscosity and Molecular Weight of CMC

Viscosity of degraded samples was examined with a rotary viscometer made by Tokyo Keiki Co. Ltd., Japan, after dilution to a 1% concentration. Weight-average molecular weights of the polymers were determined on the basis of the Mark-Houwink equation $[\eta] = K \times DP^a$, where DP is the weight-average degree of polymerization. To calculate molecular weight, it was multiplied by the average mass of the substituted anhydroglucose unit. The intrinsic viscosity was measured by a Ubbelohde viscometer in a 0.1M NaCl aqueous solution at 25°C. The time of flow of the solvent was 93.2 sec. For this conditions the constants K and a are equal to 1.8×10^{-2} and 0.97, respectively.¹²

Biodegradation Method

Enzymatic degradation was carried out using a Cellulase C-0901 enzyme (obtained from Sigma Chemical Co., USA) in an acetic acid-NaOH buffer of pH 5.0 at 37°C. After extraction of the soluble part, gel samples of about 100 mg were

Table I Degree of Substitution (DS) and Weight-Average Molecular Weight (M_w) of Carboxymethylcellulose Used

DS ^a	$[\eta]$ ^b	(M_w) ^b
0.71	—	—
0.86	6.8	4.2×10^5
1.29	7.4	5.4×10^5
1.32	7.0	5.1×10^5
2.2	5.9	5.2×10^5

^a Provided by the producer.

^b See methods for details of $[\eta]$ and M_w determination.

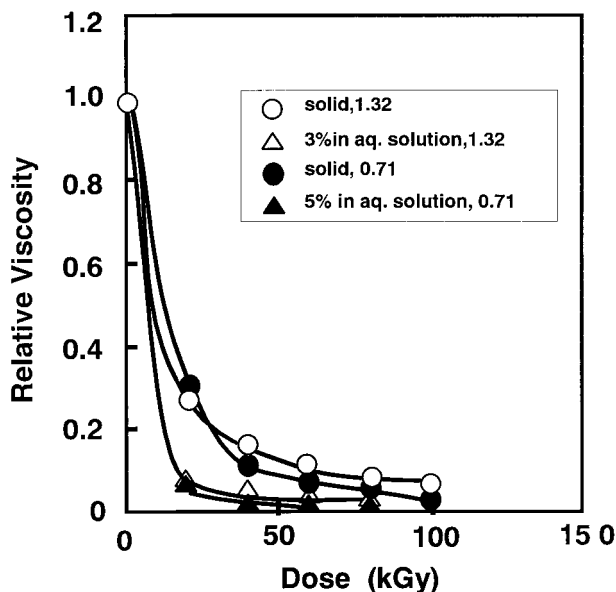


Figure 1 Viscosity of irradiated CMC with different degrees of substitution; irradiation, in air.

incubated in the enzyme solution at different times. Concentration of the enzyme in buffer was 0.1 mg mL^{-1} . Washing with distilled water and drying in a vacuum at 35°C to a constant weight followed incubation with the enzyme. The result of degradation is expressed as a percentage of weight loss

$$\text{Weight loss \%} = (W_0 - W_1)/W_0 \times 100\% \quad (3)$$

where W_0 and W_1 are, respectively, the weights of gel before and after enzymatic treatment.

RESULTS AND DISCUSSION

Degradation of CMC

To elucidate the effect of irradiation, CMC with a degree of substitution (DS) of 1.32 and of 0.71 was irradiated in solid phase and in a diluted aqueous solution up to 3% and 5%, respectively. The viscosity of the irradiated CMC is shown in Figure 1. It can be seen that there's an extreme reduction in viscosity at the early stage, up to 20 kGy, and then there's a gradual decrease with an increasing dose. It is apparent that these irradiation conditions lead to the degradation of CMC. Furthermore, even CMC with a high DS (2.2) degrades in the solid state during irradiation. Polysaccharides such as starch, alginate, and chitosan

degrade by scission of the glycosidic bond. CMC, a cellulose derivative, also degrades in this manner.

Crosslinking of CMC

CMC aqueous solution was irradiated at a high concentration (5–50%) to produce crosslinks. The gel fraction of CMC with a DS of 1.32 against delivered dose is illustrated in Figure 2. CMC aqueous solution of 20% forms a gel fraction of 55% at 30 kGy. Maximum gel fraction was achieved at concentrations from 20% to 30%, while a high concentration, such as 50%, gives a low gel fraction. CMC at concentrations of 20% and 30% have a pastelike texture. It is important for crosslinking that the polymer is homogeneously dissolved in water. For a high concentration, 50%, it was observed that water is not homogeneously dispersed into CMC.

There are two ways of water contributing to the crosslinking of CMC. First, it enhances mobility of the rigid molecules of CMC, allowing the diffusion of macroradicals to close the distance between each other and consequently for them to recombine. Second, it induces an increase of radical concentration by the products of water radiolysis. Among them, hydrogen atoms and hydroxyl radicals are the most reactive species.

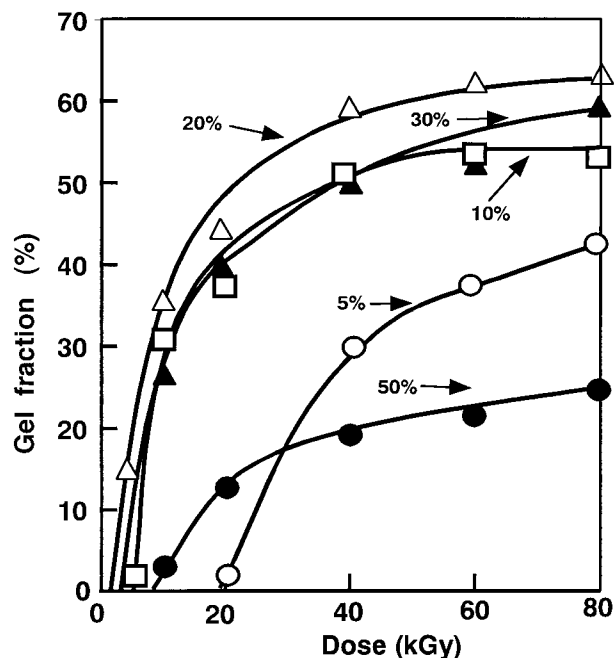


Figure 2 Effect of concentration on crosslinking of CMC; degree of substitution of CMC, 1.32; irradiation, in air.

These radicals can create CMC macroradicals by abstracting H from the polymer chain. Hence, the presence of water enhances the yield of macroradicals. Crosslinking of CMC was achieved from a direct effect of irradiation when radiation interacts directly with polymer chains and from an indirect effect when it interacts byproducts of water radiolysis. Natural rubber particles dispersed in latex undergo crosslinking, by the action of the indirect effect of water, at a lower dose as compared to the crosslinking of dry rubber.¹³ Poly(vinyl alcohol) (PVA) does not crosslink in solid phase at room temperature (25°C) because of a high glass-transition temperature, 90°C. At room temperature, molecular mobility is limited; only the vibration of atoms, chemical bonds, and the movements of small chemical groups are possible. But above the glass-transition temperature, in the elastic state, molecular movements of all chains or their parts take place. PVA at a swollen state in an aqueous solution undergoes crosslinking because of high mobility of the molecular chain, the same as in the elastic state, and from the indirect effect of radiation.^{14,15,16} The results shown in Figure 1 confirm that CMC degrades at a lower concentration, below 5%. Chains of CMC at low concentrated aqueous solutions are separated by water and placed at a distance from each other, which prevents intermolecular reactions from occurring. Then the yield of the crosslinking

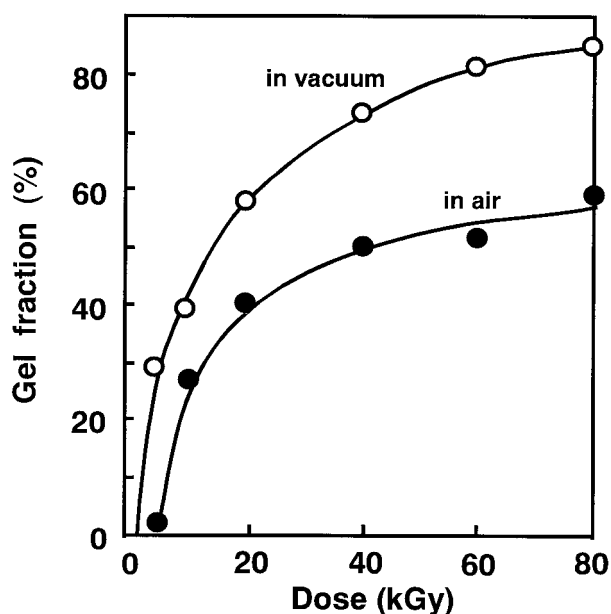


Figure 3 Crosslinking of CMC irradiated in air and vacuum; CMC concentration, 30%.

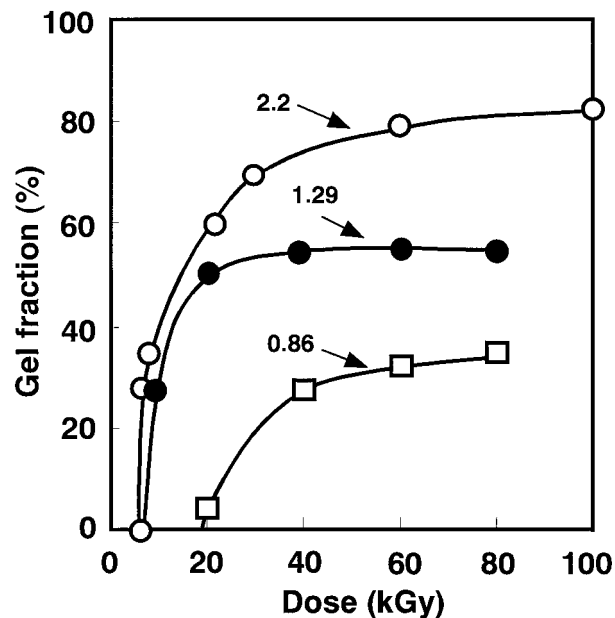


Figure 4 Effect of degree of substitution on crosslinking of CMC; Concentration of CMC, 20%; Irradiation, in vacuum.

is trivial, and the leading radiation-induced reaction is scission of glycosidic bonds. CMC solutions of moderate concentration, such as 20–30%, with a DS of 0.7, achieve a lower gel content even at a high dose, 60 kGy. Therefore, the crosslinking process occurs much easier for CMC with a higher DS and at a high concentration.

The effect of atmosphere on crosslinking of CMC was investigated. As shown in Figure 3, CMC irradiated under vacuum at 30% aqueous solution gives a higher gel fraction than that processed with air access. A gel of 82% is obtained by irradiation under vacuum at 80 kGy. Diffusion of air into the mass of the sample during irradiation was prevented by the use of poly(vinylidene chloride) packaging.

Figure 4 shows the influence of DS on the results of crosslinking of CMC irradiated in a 20% aqueous solution. The CMC with a DS of 2.2 gives the highest gel fraction among the three samples. A higher DS is effective for crosslinking of this polymer; hence, it can be concluded that intermolecular linkages are a result of ether function.

Radiation Yield and Gelation Dose

Since crosslinking and scission occur simultaneously in the polymer during irradiation, the yield of crosslinking, $G(x)$, and degradation, $G(s)$,

Table II Gelation Dose (D_g), Crosslinking $G(x)$ and Scission $G(s)$ Yields of Irradiated CMC

DS	D_g ^a	$G(x)$ ^b	$G(s)$ ^b
2.2	5.8	1.6	1.5
1.29	7.8	1.14	2.26
0.86	18.7	0.61	1.68

^a Gelation doses were determined by gel-sol analysis.

^b G values were calculated by Charlesby-Rosiak eq. (4), and eq. (5), indicated in text.

have an influence on the result of irradiation. The G value is the number of crosslink bonds or scission acts per 100 eV of absorbed energy. The yield values and gelation doses, D_g , were estimated by gel-sol analysis on the basis of the Charlesby-Rosiak equation^{17,*}

$$s + \sqrt{s} = \frac{p_0}{q_0} + \left(2 - \frac{p_0}{q_0}\right) \frac{D_v + D_g}{D_v + D} \quad (4)$$

and

$$G(x) = \frac{4.8 \times 10^5}{\bar{M}_{w0} \times D_g} \quad (5)$$

where p_0 and q_0 are degradation and crosslinking density, respectively; D is the absorbed dose and D_v is the virtual dose—a dose required for changing the distribution of the molecular weight of the polymer in such a way that the relation between weight-average and number-average molecular weight would be equal to 2; and $G(s)/G(x) = 2p_0/q_0$ (detailed explanation in the references).^{17,18} The results obtained are shown in Table II. It can be seen that radiation yield from the crosslinking of CMC with a DS of 2.2 is the highest with scission occurring the least. Among different types of CMC that were substituted, crosslinking took place the most effectively for the one with the highest DS (2.2). The gelation dose—minimum energy required to start the gelation process—is also the lowest for CMC with a DS of 2.2, increases slightly for a DS of 1.29, and is the lowest for a DS of 0.86. Comparing these data to the results obtained for PGA⁷ and PAsp,⁹ where D_g were 20 kGy and 32 kGy, respectively, we can

* Calculations were done by specially designed computer program kindly obtained from Dr. J. M. Rosiak of the Institute of Applied Radiation Chemistry, Lodz, Poland.

postulate that CMC requires less energy to produce gel. PGA and PAsp form gel at concentrations as low as 2% (neutral pH, number-average molecular weight 1.25×10^6) and 5% (basic solution, weight-average molecular weight 9.5×10^4), respectively. The critical concentration of the latter is the same as CMC with a DS of 2.2, but the molecular weight of PAsp is 5.5 times less.

The relationship between DS and concentration of CMC in aqueous solution (Figs. 2 and 4) and their influence on the crosslinking are summarized in Figure 5. Crosslinking of CMC with a high DS occurs at a relatively lower concentration, 5%, while for a low DS, a high concentrated solution is required to produce gel.

Swelling and Biodegradability

The basic feature of hydrogel is its ability to absorb and hold huge amount of solvent in its network structure. Figure 6 shows the swelling of hydrogel, made from CMC 20% aqueous solution, in deionized water and 0.9% NaCl. The swelling (weight of deionized water absorbed per gram of dried gel) decreases with an increasing dose. This is because of the increase in crosslinking density of the hydrogel. The gel shows the maximum swelling of 165 and of 78 in water and in 0.9% NaCl aqueous solution, respectively. Commercial hydrogel of sodium acrylate grafted onto starch was reported to have a swelling of 360 in deionized water and 60 in 0.9% NaCl. There has been a

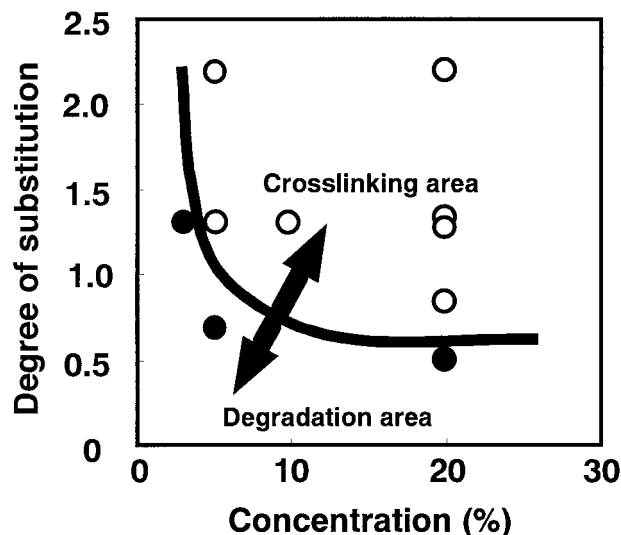


Figure 5 Relationship between degree of substitution and concentration in aqueous solution for radiation crosslinking of CMC.

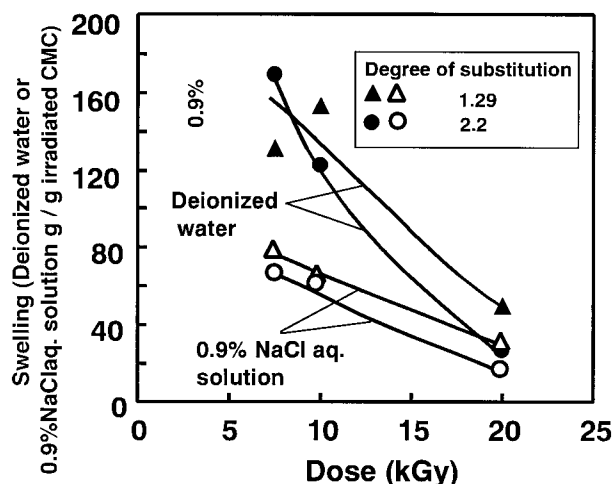


Figure 6 Swelling of irradiated CMC in deionized water and 0.9% NaCl aqueous solution; concentration of CMC, 20%.

recent report of new biodegradable hydrogels made from poly(amino acid), such as poly(glutamic acid)⁷ (PGA) and poly(aspartic acid)⁹ (PAsp), and prepared by γ irradiation. These polymers have high swelling, 3000 in deionized water but only 27.4 in artificial urine (nearly 0.9% NaCl aqueous solution). Swelling of a crosslinked CMC–NaCl solution is higher than are those of crosslinked poly(amino acid) and sodium acrylate grafted onto starch. The swelling is a very important factor considering the probable application of hydrogels as diapers.

The biodegradability of CMC gel (100% of gel, after extraction of sol part) was evaluated by enzymatic degradation. We found that highly crosslinked CMC (delivered dose of 70kGy) degrades to 15% after 80 h of incubation with the enzyme. Compared to PCL, where biodegradation by the lipase enzyme was considerably retarded by the presence of crosslinks,¹⁵ CMC can degrade even after its chains become crosslinked. The biodegradation of CMC is still under detailed study. We expect CMC hydrogel formed by high-energy radiation at lower doses such as 30 kGy, which is appropriate for high swelling, will degrade much faster than the present example. It will be discussed in subsequent reports.

CONCLUSION

A novel biodegradable hydrogel of carboxymethylcellulose was synthesized without any addi-

tives. A high DS and concentration in aqueous solution were very effective for the crosslinking of CMC. A 20% solution of CMC with a DS of 1.32 was found to be favorable for crosslinking. A pastelike mixture of CMC with water is preferable for hydrogel preparation. A preliminary enzymatic degradation study confirmed that CMC hydrogel could be included into the group of biodegradable polymers. CMC hydrogel is expected to be useful as a cosmetic, medical, agricultural, and hygienic materials component.

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