

Physical characterization and molecular structure of hydrophilic polymers obtained by radiation cast-polymerization of methoxypolyethyleneglycole methacrylate monomers for biomedical applications

MINORU KUMAKURA, ISAO KAETSU

Takasaki Radiation Chemistry Research Establishment, Japan Atomic Energy Research Institute, Takasaki, Gunma, Japan

Hydrophilic polymers were prepared by radiation cast-polymerization of methoxypolyethyleneglycole methacrylate monomers for biomedical applications, and the relationship between physical characterization and molecular structure was studied. As the number, n , of oxyethylene units, $-(\text{OCH}_2\text{CH}_2)_n-$, in the monomers increased, the hydration ability of the polymers increased markedly until $n = 4$ and after that increased moderately. The mechanical properties, such as tensile and tear strength decreased, and the elongation at break increased to a maximum and then decreased with increasing n . This appeared to be a characteristic of the polymers of methoxypolyethyleneglycole methacrylate monomers. The mechanical properties of the copolymers resulting from the copolymerization of methoxypolyethyleneglycole methacrylate with hydroxyhexyl methacrylate monomer were also studied.

1. Introduction

Hydrophilic polymers (hydrogel materials) have had various applications in the biomedical and biological fields. The most useful description is that hydrogels are water swollen polymer networks of either natural or synthetic origin and of these, it is the cross-linked, covalently bonded, synthetic hydrogels that have grown most dramatically in use. The recent developments and interest in the field can be traced back to the studies of Wichterle and his co-workers [1] who first indicated the usefulness in biomedical applications of the polymers of 2-hydroxyethyl methacrylate (HEMA). The amount of water absorbed expressed as equilibrium water content is the most significant property of the gel since it has a profound effect on the permeability, mechanical properties, surface properties and biocompatibility of the resultant material [2-4]. Hydrogels have been considered as vehicles for the immobilization, encapsulation,

and controlled release of many physiologically active substances including antibiotics, anticoagulants, anticancer drugs, antibodies, drug antagonists, enzymes, contraceptives, and antibacterial agents. Because of the water swollen network structure of hydrogels and the fact that the constituent monomers are hydrophilic, biologically active components may be either physically entrapped or covalently bound within the gel. Both these methods can be used to give temporary or permanent immobilization [5].

The water content of hydrogel is affected by the nature of the hydrophilic monomers used in preparing the polymer or copolymer and the nature and density of the cross-links. Copolymerization with more hydrophilic monomers enables hydrogels having water contents greater than 40% to be produced. At the more hydrophilic end of the range, the uncross-linked polymers are water soluble and the water contents of the

derived gels are markedly dependent upon cross-link density. The relationship between molecular structure and water content is important and shows many interesting features.

In this paper, we studied highly hydrophilic polymers in which the polymers are obtained by radiation cast-polymerization of methoxypolyethyleneglycole methacrylate monomers, and have studied the relationship between physical characterization and molecular structure of its polymers.

2. Experimental procedure

2.1. Monomers

Methoxypolyethyleneglycole methacrylate ($\text{CH}_2\text{C}(\text{CH}_3)\text{CO}(\text{OCH}_2\text{CH}_2)_n\text{OCH}_3$, M- n G) monomers were used, in which M-4G and M-9G were purchased from Mitsubishi Gas Chemical Co. Ltd, and other monomers ($n = 1, 2, \text{ and } 3$) and hydroxyhexyl methacrylate (HHMA) were synthesized in our laboratories by an esterification reaction using *p*-toluensulphonic acid as a catalyst. The monomers synthesized were purified by base extraction to remove any inhibitors, followed by distillation. The purity of the monomers, which was determined by gas chromatography, was 99%.

2.2. Radiation cast-polymerization

Radiation cast-polymerization of M- n G was carried out using a casting flame as follows. The monomer was charged in the casting flame which was constructed of two glass plates, a silicone-rubber gasket, and flame fixing clamps. After charging the monomer, the casting flame was irradiated (total dose, 1×10^6 rad) by γ -rays from ^{60}Co source, at a dose rate of 1×10^6 rad h^{-1} at room temperature. After irradiation, the polymeric membrane was obtained by releasing the flame fixing clamps. Polymeric membranes having different thicknesses can be obtained by regulation of the thickness of the silicone-rubber gasket.

2.3. Measurements

Tensile strength and the elongation at break were determined by using specimens cut into dumbbell shapes according to ASTM D-638, and tear strength test was carried out according to ASTM D-1004 with an Instron universal testing instrument (model 1130).

A water swelling experiment was performed by immersing the membrane into distilled water at room temperature for one week. Water content (%) was determined as the ratio of weight of water

to the weight of the membrane at swelling equilibrium at 25°C , and water absorption (%) was determined as the ratio of weight of water to the weight of the membrane when dry. Contact angles were measured using a contact angle goniometer. An average of at least six measurements was taken for each polymer examined.

3. Results and discussion

3.1. Hydration property and molecular structure

The hydration properties of M- n G polymers were examined. The relationship between water content or water absorption and the number, n , of oxyethylene units, $-(\text{OCH}_2\text{CH}_2)_n-$, in M- n G is shown in Fig. 1. As n increased, the water content and absorption of the polymers increased markedly till $n = 3$ and after that increased moderately. This result shows that the hydration property of the polymers is related intimately to the number of oxyethylene units in the monomer, in which the hydration part in the polymers attributes to the ether bond of a polar group. Thus, the increase of the hydration ability of the polymers with increasing n is due to the increase of the number of ether bonds. However, the water content and absorption curves in Fig. 1 did not show a linear dependence on n , suggesting that hydration ability is affected by polymer structure such as configuration of the polymer chain and crystallinity. Thus, it was found that hydration ability of the polymers does not appear to be linearly dependent on the number of polar ether bonds.

McLaren and Rowen reported that the sorption of water vapour by polymers did not show a linear increase with the increase of the number of polar groups [6]. In the M- n G polymers, it is suggested that the mechanism of water absorption relates to polymer structure. The water content of the hydroxyalkyl methacrylate polymers decreased with increasing numbers of methylene units [7], while in the hydroxypolyethyleneglycole methacrylate polymers, water content increased till $n = 2$ and after that was constant with increasing numbers of oxyethylene units [8], and this feature was similar to that in the M- n G polymers. The molecular structure dependence of the hydration ability in polymers consisting of monomers which have an oxyethylene unit, appeared to be similar to each other. This apparently shows that the oxyethylene unit in the polymer chain has a complex effect on its hydration. The hydration ability

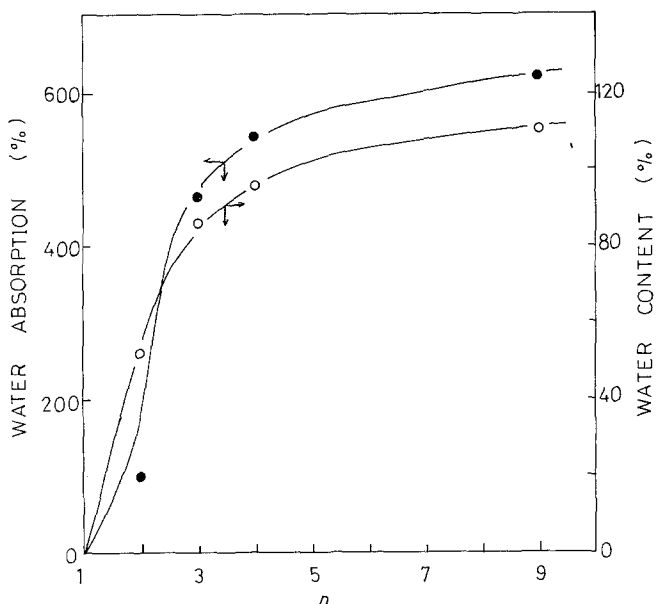


Figure 1 Relationship between water content or water absorption and the number of oxyethylene units in the M-*n*G polymers.

of polymers having oxyethylene units should be depressed by factors such as intra-molecular hydrogen bonding. The water contents of M-*n*G polymers ($n > 2$) were larger than those of hydrogels and were comparable with those of soft contact lens materials [9, 10].

The relationship between contact angle and n is shown in Fig. 2. The contact angle of the polymers of M-*n*G decreased to 1 to 2° at $n = 4$ and after that was constant with increasing n , indicating that the polymers of $n > 4$ have very high hydrophilicity. The contact angle shows the wettability of the surface of polymer and seemed to be different from the degree of hydration, which is obtained

from an equilibrium swelling in water. The value of the contact angle of the M-3G polymer in Fig. 2 is smaller than those of other hydrophilic polymers such as poly(vinyl alcohol), polyHEMA, etc, though the water content of poly(vinyl alcohol) was comparable with that of the polymer of M-3G. From this result, it is suggested that the surface of the M-*n*G polymers has high cohesion energy and wettability. Such properties are available for biomedical and biological applications, taking a biocompatible property. As reported previously, M-*n*G ($n > 3$) was a suitable monomer in the immobilization of biological substances such as erythrocytes, cells, etc. [11].

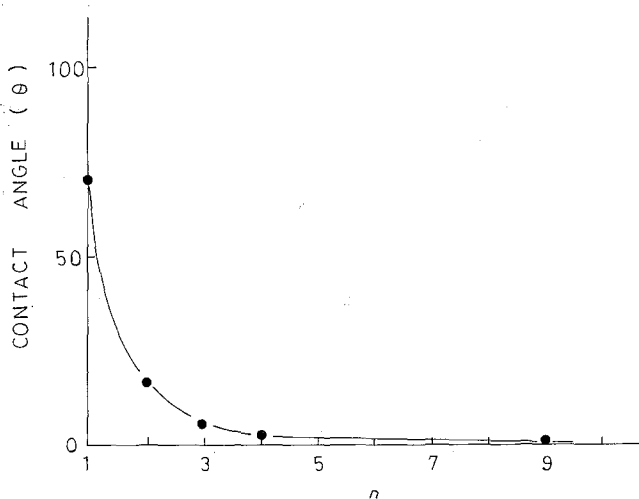


Figure 2 Relationship between contact angle and the number of oxyethylene units in the M-*n*G polymers.

3.2. Mechanical properties and molecular structure

The mechanical properties of the M- n G polymers were studied. The relationship between tensile strength and n is shown in Fig. 3. The tensile strength decreased markedly with increasing n , but this decrease was moderate above $n = 4$. A remarkable decrease of the tensile strength at smaller n indicates that the molecular structure varies markedly with n . In fact, the hydration ability was also increased at smaller n as shown in Figs. 1 and 2. In the short length of the polymer chain, the flexibility of the polymer appeared to greatly increase with increasing n . This feature was different from that in hydroxyalkyl methacrylate polymers, where the tensile strength increased to a maximum and then decreased with increasing number of methylene units [8]. Thus, it was found that the tensile strength in M- n G polymers was very different from that in hydroxyalkyl methacrylate polymers. The tensile strength of the M-2G or M-3G polymer was comparable with

that of polyHEMA which is used for contact lenses [12]. The tensile strength of the M-1G polymer was large and comparable with that of poly(vinyl chloride), which has medical uses [13]. Since the tensile strength of the swollen polymer of M-1G is relatively large, it could be considered for medical applications.

The decrease of the tensile strength by swelling of the polymer in water was relatively small as can be seen in Fig. 3. This characteristic is very important in biomedical applications. In general, it is known that the tensile strength of hydrophilic polymers is decreased by swelling, e.g. the tensile strength of polyHEMA was decreased about one-tenth by swelling in water. This swelling phenomenon (hydration) is a complicated process occurring mainly between polymers and water. The polymers of M- n G when hydrated would retain a tensile strength with mutual interaction of the polymer chain.

The relationship between tear strength and n is shown in Fig. 4. The variations of the tear strength

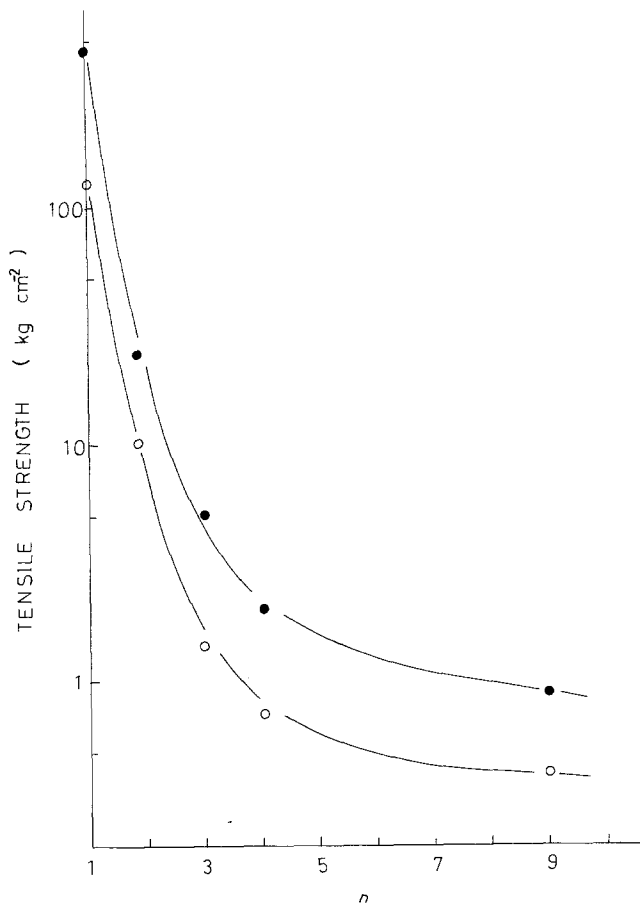


Figure 3 Relationship between tensile strength and the number of oxyethylene units in the M- n G polymers: ● non-swollen polymer, ○ swollen polymer.

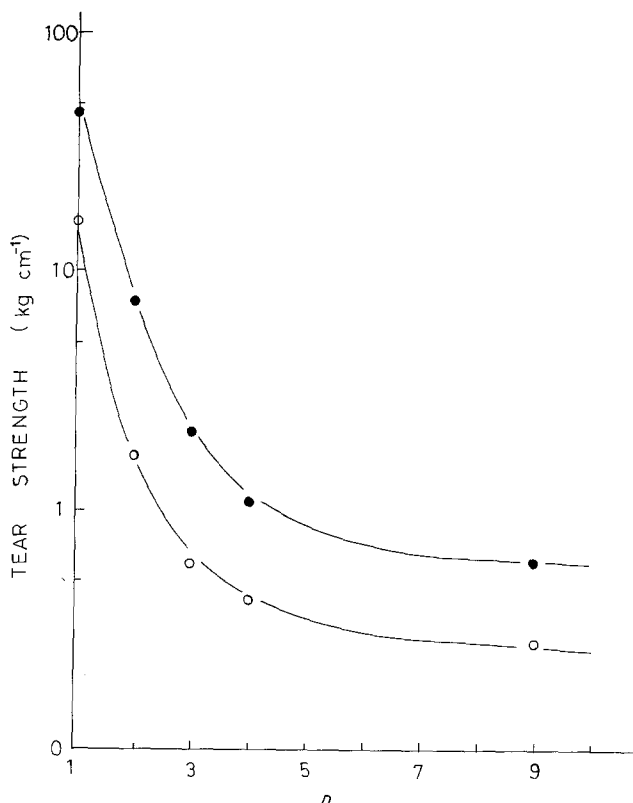


Figure 4 Relationship between tear strength and the number of oxyethylene units in the M-*n*G polymers: ● non-swollen polymer, ○ swollen polymer.

with n is similar to that of the tensile strength, i.e. the tear strength decreases markedly with increasing n at smaller n .

The relationship between the elongation at break and n is shown in Fig. 5. The elongation at break increased markedly to a maximum and then decreased and after that was almost constant with increasing n . This variation of the elongation at break with n appeared to be of interest with regard to the molecular structure of the polymer, and it seemed to be correlated with the form of the hydration ability and tensile strength in Figs. 1 and 3. The curve in Fig. 5 appeared to be just the differential curve of those in Figs. 1 to 4. The result in Fig. 5 shows that the M- n G polymers having smaller n , i.e. $n = 2$ or 3, are highly flexible and have a sufficient strength, and that the polymers of M- n G having larger n , i.e. above $n = 4$, have low flexibility and have a low strength. The elongation at break of the polymer of M-3G was comparable with that of polyHEMA used for contact lenses [9]. The elongation at break of the M-2G polymer was relatively large and comparable with that of poly(vinyl chloride) used for medical purposes and slightly smaller than that of silicone rubber [13]. The elongation at break of

the M- n G polymers ($n > 4$) seemed to be larger than those of other hydrogels such as poly(N-vinyl pyrrolidone), and these polymers could be used for various biomedical applications by copolymerization with other monomers.

3.3. Mechanical properties of copolymers from M- n G and HHMA

The mechanical properties of the polymers obtained by copolymerization (monomer ratio; 1:1) of M- n G with HHMA were studied. The relationship between tensile strength of the copolymers decreased markedly with increasing n , in which the tensile strength of the copolymers from smaller n ($n < 3$) and larger n ($n > 3$) decreased and increased by copolymerization (Fig. 6). Furthermore, the difference between the values of the tensile strength of swollen and non-swollen polymers decreased by copolymerization, indicating that the hydration ability of the copolymers decreases. From this result, it was found that the tensile strength of the polymers of M- n G ($n > 3$) can be improved by copolymerization with HHMA: the HHMA polymer had a hydrophobic and elastic property. The relationship between the elongation at break and n is shown in Fig. 7. The elongation- n curve in the

Figure 5 Relationship between the elongation at break and the number of oxyethylene units in the M-nG polymers.

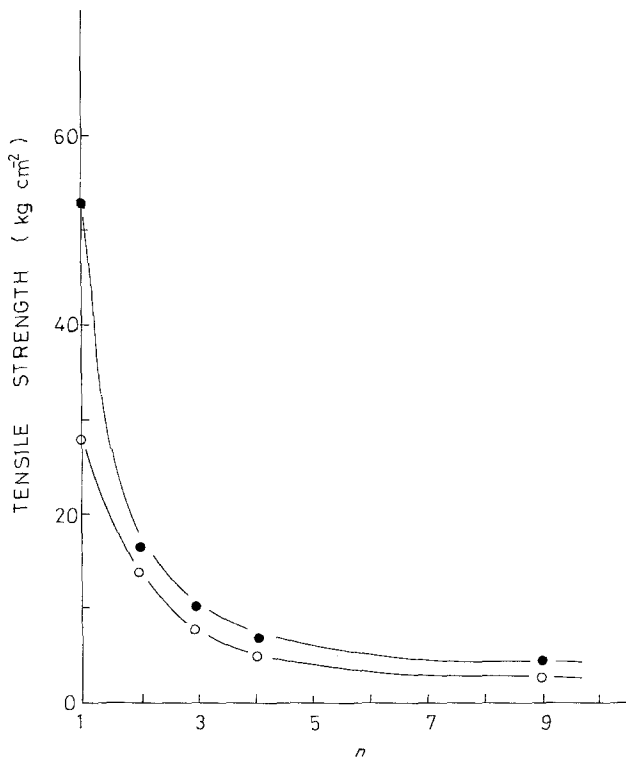
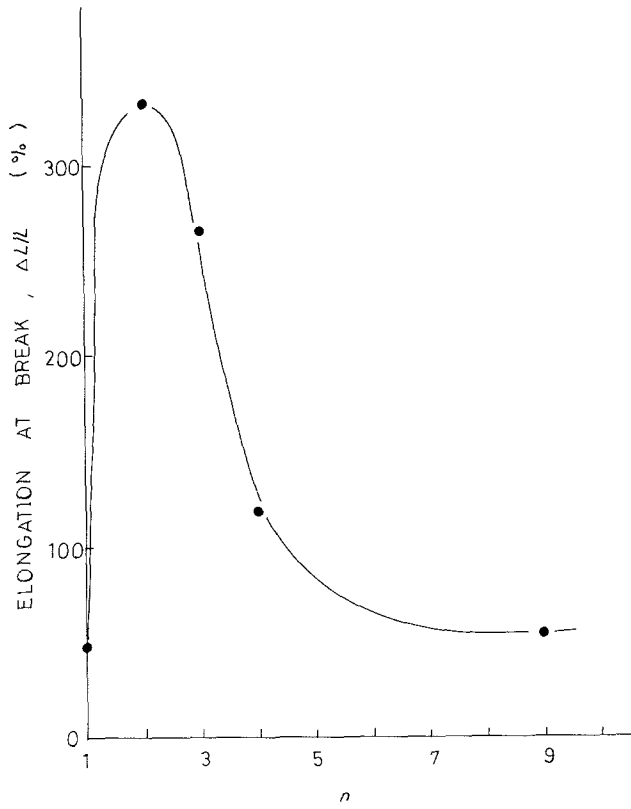


Figure 6 Relationship between tensile strength and the number of oxyethylene units in the copolymers of M-nG and HHMA: ● non-swollen copolymer, ○ swollen copolymer.

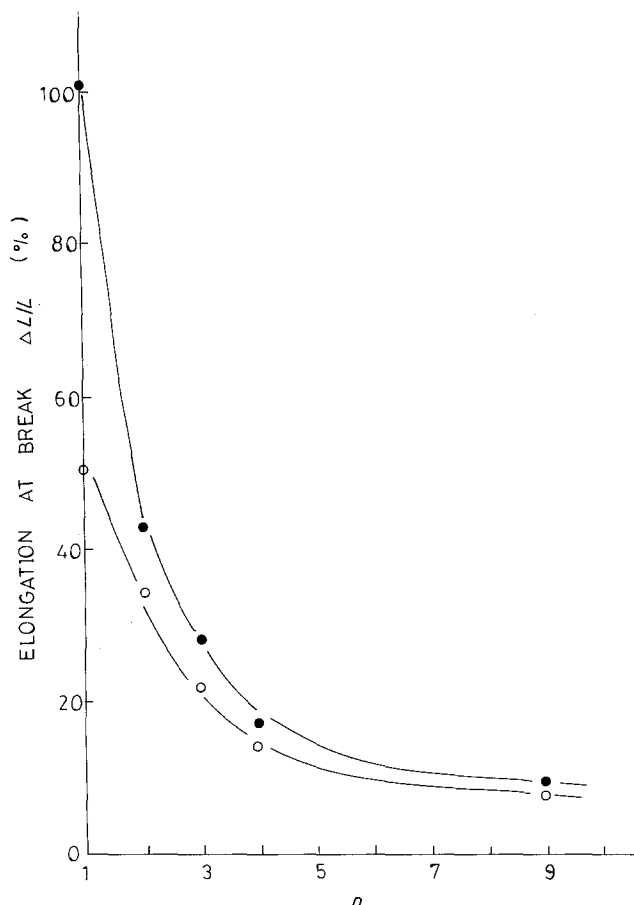


Figure 7 Relationship between the elongation at break and the number of oxyethylene units in the copolymers of M-nG and HHMA: ● non-swollen copolymer, ○ swollen copolymer.

copolymers shows a monotonic decrease and it was different from that of the M-nG polymers alone. This resulted in the increase of the elasticity in the M-1G polymer due to copolymerization. The elongation at break of the polymers of M-nG ($n > 4$) decreased by copolymerization though the tensile strength increased. Thus, the copolymerization of M-nG with hydroxyalkyl methacrylates which have long alkyl chains introduced in the polymers of low elasticity and slight stiffness. These copolymers, which are transparent materials, seemed suitable for various medical applications.

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