

Preparation of Hydrogel Beads from Crosslinked Poly(Methyl Methacrylate) Microspheres by Alkaline Hydrolysis

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Synopsis

Poly(methyl methacrylate)/(PMMA) microspheres crosslinked with various concentrations of ethylene glycol dimethacrylate (EGDM) were prepared by a suspension polymerization procedure. They were subjected to alkaline hydrolysis in ethylene glycol at high temperature ($> 175^{\circ}\text{C}$), resulting in the rapid conversion of methacrylate ester functions to methacrylic acid, while retaining the spherical shape of the microspheres intact. The method provides a novel approach to obtain smooth, nearly perfect spherical, mechanically strong, high-water-absorbing hydrogel beads from crosslinked PMMA. The reaction has been found to be considerably faster than many of the hydrolysis procedures reported previously. The effect of concentration of alkali, particle size, crosslinking density, and reaction time on the extent of hydrolysis has been investigated to a limited extent.

INTRODUCTION

Polymeric acids such as poly(methacrylic acid) and poly(acrylic acid) find application as adhesives, thickeners, fluidizers, coatings, flocculants, dispersants, and ion-exchange resins.¹ In addition to the polymerization of the appropriate monomer, acid or alkaline hydrolysis of the corresponding ester polymer constitutes an important method for their preparation.² While the acrylic ester polymers are hydrolyzed relatively easily, the corresponding methacrylate polymers are more resistant to hydrolysis.³ However, modified hydrolyses such as the use of molten caustic or a heterogeneous system of sodium hydroxide and aqueous isopropanol can hydrolyze the methacrylate ester polymers. The reactions are usually time-consuming. Thus, conventional, isotactic and syndiotactic PMMA have been subjected to alkaline hydrolysis in aqueous mixtures of isopropanol.⁴ The conventional polymer, for example, undergoes 50% hydrolysis in 140 h whereas the isotactic polymer undergoes 75% hydrolysis under identical conditions. The preparation of carboxylated methacrylate polymers by alkaline hydrolysis using 30–50% alkali metal hydroxide in aqueous mixtures of cyclohexanol is disclosed in a recent German patent.⁵ Preparation of crosslinked poly(sodium acrylate) and poly(sodium methacrylate) beads by suspension polymerization as water absorbing agents has been reported recently.^{6,7}

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To the best of our knowledge, all the hydrolysis procedures reported so far have been confined to the uncrosslinked polymer usually resulting in a low degree of hydrolysis even with prolonged reaction times. We have attempted here to hydrolyze crosslinked PMMA microspheres in ethylene glycol (EG) at high temperatures with the aim of preparing discrete, spherical, hydrogel beads with high water-absorbing capacity. The method provides a novel way to obtain smooth, spherical hydrogel beads of large size from crosslinked PMMA. The reaction is also considerably faster than many of the hydrolysis procedures previously reported. The hydrolyzed PMMA beads have been demonstrated to be useful as artificial emboli^{8,9} and as a microcarrier for the culture of mammalian cells.¹⁰ They may also find application as water absorbing agents and as ion-exchange resins.

EXPERIMENTAL

Preparation of Crosslinked PMMA Microspheres

Crosslinked PMMA microspheres were prepared by a modified dispersion polymerization procedure of Hart.¹¹ Thus polyacrylamide (BDH, U.K., mol wt 5.0×10^6) (1.0 g), poly(vinyl alcohol) (BDH, U.K., mol wt 1.25×10^3) (4.0 g), $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ (T. Baker, India) (1.0 g), and $\text{NaH}_2\text{PO}_4 \cdot 2\text{H}_2\text{O}$ (T. Baker, India) (0.5 g) were dissolved in 300 mL of distilled water in a 500-mL three-necked round bottomed flask fitted with a water condenser, thermometer, and a stainless steel half-moon stirrer. To this mixture was added with stirring, 60 mL of distilled, inhibitor-free MMA (BDH, U.K.), the required amount of EGDM (Aldrich, U.S.A) and 0.6 g of benzoyl peroxide (BDH, U.K.). The suspension was stirred at a speed of 200 rpm ($\pm 10\%$) and heated to 70°C over a period of 1 h and the stirring was continued for another 3 h at 70°C. The polymer formed was filtered, washed several times with distilled water, and dried in an air oven at 70°C. Microspheres of different size ranges were then separated by sieving the polymer in test sieves (Filterwel, India).

Hydrolysis Procedure

The crosslinked PMMA microspheres were then hydrolyzed using KOH (LR, Glaxo, India) in EG (LR, 95%, Glaxo, India) for various periods of time. A 100-mL round-bottomed flask fitted with a condenser and a thermometer was charged with 50 mL of EG containing 5 or 10% KOH. The contents were then heated in an oil bath kept over a magnetic stirrer and the mixture was stirred using a Teflon-coated magnetic stirring bar. Once the solution started boiling, 1 g of PMMA microspheres was introduced and the heating continued. With 5% KOH, the solution boiled at 180–183°C whereas, with 10% KOH, the refluxing temperature was 175–176°C. The reaction was quenched at various time intervals by pouring the contents into a large volume of water. The hydrolyzed microspheres were then filtered, washed, and equilibrated in water for several days.

Determination of Carboxyl Content of Hydrolyzed Microspheres

Hydrolyzed microspheres were washed in distilled water for 5 days and dried. Three tenths of a gram of the dried material was weighed accurately into a 150 mL conical flask and 20 mL of approximately 0.2N HCl of known strength was added and the flask stoppered. Contents were allowed to stand for 20 h with occasional shaking. Five milliliters of the acid was then pipetted out from the flask without the beads and titrated against NaOH of 0.1N strength. The carboxyl content was then calculated from the titre values. Experiments were done in duplicate. Reproducibility of titre values was always within $\pm 1\%$.

Equilibrium Water Content (EWC) of Hydrolyzed Microspheres

The EWC (%) of the hydrolyzed microspheres was determined as follows. A known amount of the dry material was equilibrated in distilled water overnight. Excess water was removed using a Pasteur pipette having a narrow orifice through which the swollen beads would not pass. The weight of the swollen beads was determined and the EWC was calculated using the following relation.

$$\text{EWC}(\%) = 100 \times \frac{\text{wt swollen beads} - \text{wt dry beads}}{\text{wt swollen beads}}$$

All swelling experiments were performed at 30°C. Values reported are the average of three determinations.

Swelling Ratio of Hydrolyzed Microspheres

The swelling ratios were determined from the weights of the swollen and dry beads and their corresponding densities using the following relation¹²:

$$\text{swelling ratio} = \frac{\text{wt swollen gel}}{\text{wt dry gel}} \frac{\text{density dry gel}}{\text{density swollen gel}}$$

The densities were determined using *n*-heptane as the liquid in a specific gravity bottle by the volume displacement technique.¹³

RESULTS AND DISCUSSION

Table I shows the EWC of 0.5 mol % EGDM-crosslinked PMMA beads of 180–355 μm size on treatment with two different concentrations of KOH for various time intervals. As the concentration of alkali is increased, the hydrolysis rate is also increased as evidenced by the higher water absorption capacity of the polymer. A more quantitative determination of the extent of reaction was carried out by estimating the titratable carboxyl groups generated during hydrolysis. Thus, Figure 1 shows the amount of methacrylic acid (MA) groups produced for various reaction times when 1 g of 1.0 mol % EGDM crosslinked PMMA microspheres of 180–355 μm size was subjected to hydrolysis with 5%

TABLE I
Effect of Concentration of KOH on the EWC of Hydrolyzed PMMA Beads^a

Time (min)	EWC (%)	
	10% KOH	5% KOH
15	46.23	40.35
30	74.83	61.47
45	92.91	90.25
60	96.79	94.25
70	97.68	94.85
80	98.57	95.69
90	99.26	96.06
100	99.42	96.79
110	99.42	97.07
135	—	98.63
150	—	99.35
165	—	99.85

^a Reaction conditions: 1 g 0.5 mol % EGDM crosslinked PMMA beads of 180–355 μm size in 50 mL EG.

KOH. As can be seen from Figure 1 approximately 50% of the ester functions are hydrolyzed in 90 min. In 3.5 h, however, titratable carboxyl groups generated have been estimated to be only 79.5%. The corresponding EWC of the polymer was found to be 99.4%. The relationship between the percentage MA content in the polymer and its water absorbing capacity is shown in Figure 2. There is a sharp increase in the EWC of the polymer when the MA content increases from around 20% to approximately 50%. Further increase in MA content does not drastically change the EWC of the polymer.

The effect of crosslinking on the rate of hydrolysis was studied using PMMA microspheres of different crosslinking densities with the same concentration of alkali. Table II demonstrates the data. The uncrosslinked polymer underwent the hydrolysis rapidly as compared to the polymer having different crosslinking densities. Thus, in about 1 h, the uncrosslinked microspheres were found to partially dissolve in the reaction medium whereas microspheres having crosslinking densities as low as 0.5 mol % were found to be intact, though considerable hydrolysis took place as evidenced by their EWC and MA content. The higher the crosslinking density, the slower was the rate of hydrolysis as shown in Table II, suggesting that the reaction is a diffusion-controlled process. Polymers having a higher crosslinking density swell less in the reaction medium, thereby slowing down the rate of hydrolysis. The particle size of the microspheres also exerts its effect on the hydrolysis rate. Microspheres of smaller size underwent hydrolysis faster as compared to larger size (Table III). This could be attributed to the large surface area available for the reaction in the case of smaller microspheres.

Figure 3 shows the optical photomicrographs of 1.0 mol % EGDM-crosslinked PMMA microspheres before and after hydrolysis using 5% KOH for 90 min. It is to be noted that the smooth spherical shape of the beads is not affected by the drastic reaction conditions. The uncrosslinked hydrogel beads were found to undergo dissolution in water on prolonged standing where as the crosslinked beads with water contents as high as 99% were found to be

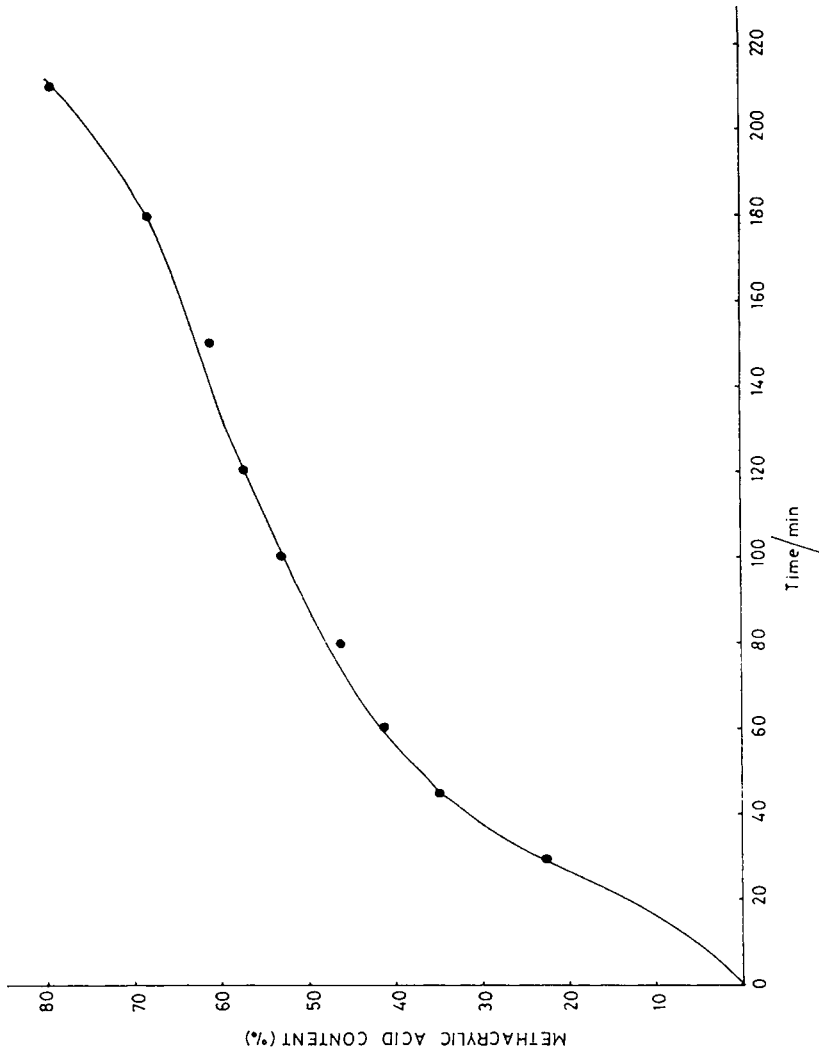


Fig. 1. Percentage MA content produced with reaction time when 1 g of 1.0 mol % EGDMA crosslinked PMMA beads of 180-355 μm size was hydrolyzed using 5% KOH in EG.

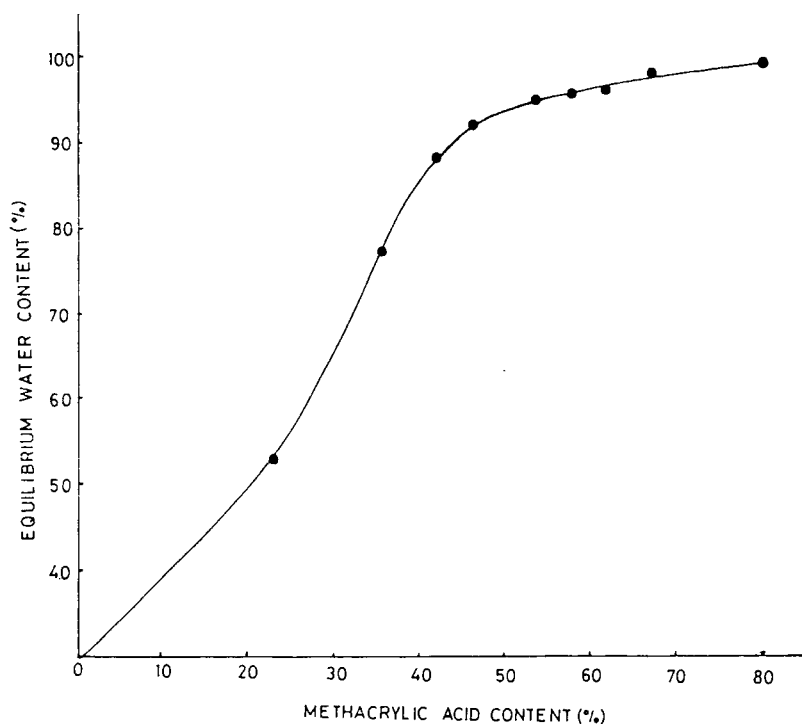


Fig. 2. Variation of EWC with MA content produced on hydrolysis in the case of 1.0 mol % EGDM crosslinked PMMA microspheres of 180–355 μm size.

TABLE II
Effect of Crosslinking on the Hydrolysis of PMMA Beads as Evidenced by Their EWC^a

Time (min)	EWC (%)				
	Uncrosslinked	EGDM (0.5 mol %)	EGDM (1.0 mol %)	EGDM (2.0 mol %)	EGDM (5.0 mol %)
5	37.21	—	—	—	—
15	72.26	40.35	44.23	35.36	—
30	97.96	61.47	53.13	—	45.40
45	99.64	90.25	77.50	65.30	—
60	99.78	94.25	88.37	80.73	70.13
70	—	94.85	90.65	85.35	—
80	—	95.69	92.13	86.54	79.54
90	—	96.06	92.50	—	—
100	—	96.79	93.29	87.71	84.60
110	—	97.07	93.86	88.36	—
120	—	97.86	94.68	89.55	87.52
135	—	98.63	95.24	90.00	—
150	—	99.35	96.11	90.30	90.79
165	—	99.85	97.47	91.14	—
180	—	—	98.44	92.08	93.46
195	—	—	99.20	94.91	95.07

^a Reaction conditions: 1 g PMMA beads of 180–355 μm size in 50 mL EG containing 5% KOH.

TABLE III
Effect of Bead Size on the Hydrolysis of 1 mol % EGDM Crosslinked PMMA^a

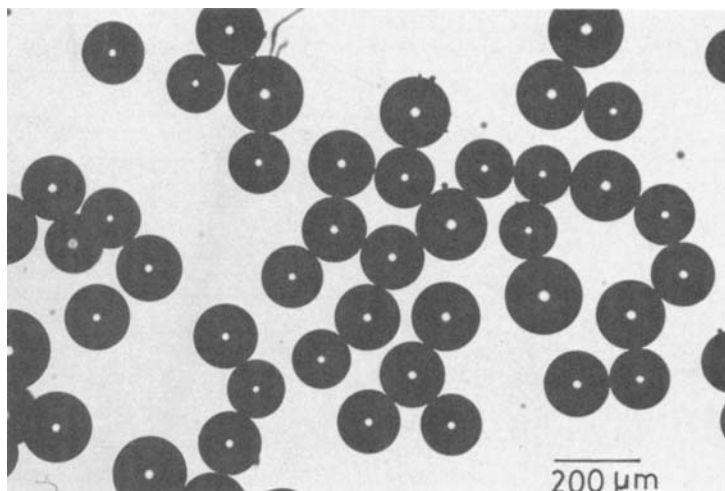
Time (min)	EWC (%)	
	180–355 μm size	125–180 μm size
15	44.23	—
30	53.13	85.14
45	77.50	92.78
60	88.37	94.77
70	90.65	95.36
80	92.13	96.42
90	92.50	97.19
100	93.29	97.65
110	93.86	98.13
120	94.68	98.80
135	95.24	99.52
150	96.11	99.73
165	97.47	99.90
180	98.44	—
195	99.20	—

^aReaction conditions: 1 g of PMMA beads in 50 mL of EG containing 5% KOH.

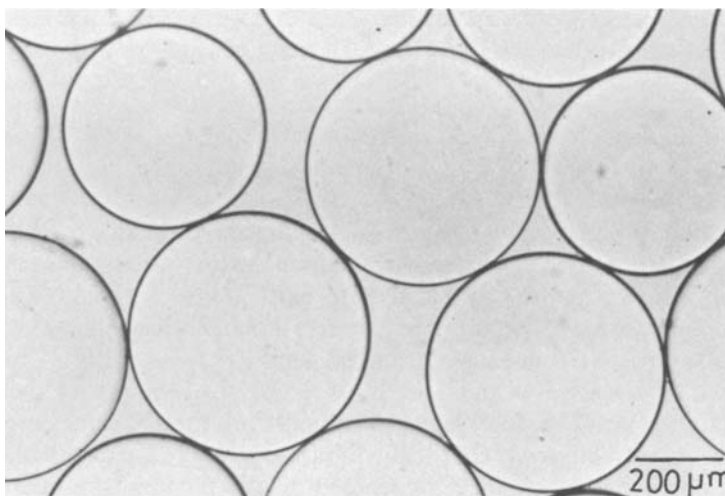
stable on prolonged standing in water, which suggests that the EGDM crosslinks are not completely hydrolyzed even under the drastic reaction conditions employed.

This method of preparation of hydrogel beads from crosslinked PMMA has the advantage that beads of required size and water content can easily be prepared in a nearly perfect spherical form by a judicious choice of reaction conditions. Suspension polymerization of acrylic or methacrylic acid usually results in a sandy mass¹⁴ lacking a spherical geometry. The method provides a simple way to obtain hydrogel beads of large size comprised mostly of poly(methacrylic acid). From the swelling ratio of these beads determined (Table IV) it can be seen that the diameter of the beads increases on hydrolysis and swelling in water by approximately 3.5 times. Since PMMA beads up to 1.0 mm in diameter can easily be prepared by suspension polymerization, hydrolysis of such beads would generate hydrogel beads which swell to more than 3 mm in diameter.

The rate of swelling of the hydrogel beads was found to be very fast and convenient for many applications. Table IV demonstrates the data. The EWC is approached in about 1 min. The density of the dry gel is high and of the swollen gel is low and approaches unity as the EWC becomes very high. It is apparent that the potassium methacrylate formed during hydrolysis of PMMA is responsible for the high-water-absorbing property of the beads. On acidification, the swelling was considerably reduced because of the conversion of the carboxylate salt to its acid. This result was confirmed by FTIR analysis. The FTIR spectrum of the hydrolyzed beads (taken in a DIGILAB 3240 spectrophotometer, KBr pellets) showed a strong peak at 1555 cm^{-1} from the carboxylate anion. On acidification, this peak shifted to 1717 cm^{-1} , which is attributable to the carboxylic acid group.¹⁵ The original EWC was regained when the beads were allowed to reequilibrate in alkaline solution.



(a)



(b)

Fig. 3. Optical photomicrographs of 1.0 mol % EGDM crosslinked PMMA microspheres of 125–180 μm size: (a) before hydrolysis and (b) after alkaline hydrolysis and swollen in water to have an EWC of 97%.

TABLE IV
Rate of Swelling of Hydrogel Beads Derived from 0.5 mol % EGDM
Crosslinked PMMA in Water

Time (s)	EWC (%)	Density (g cm^{-3})	Degree of swelling ^a	Swelling ratio
0	0	1.495	1.00	1.0
10	91.64	1.180	11.98	15.18
30	95.32	1.122	21.35	28.45
60	96.72	1.063	30.48	42.87
600	96.79	1.014	31.17	45.96

^a Degree of swelling = wt swollen gel/wt dry gel.

CONCLUSIONS

Crosslinked PMMA microspheres can be subjected to alkaline hydrolysis in ethylene glycol at elevated temperatures to give smooth, spherical, high-water-content hydrogel beads. The ease of hydrolysis depends on the crosslinking density of the beads, concentration of alkali, and particle size. Hydrolyzed PMMA beads having very high water contents were found to be stable in water, suggesting that the EGDM crosslinks are not completely hydrolyzed even under the drastic reaction conditions employed.

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