

# Preparation of Functional Polymer-Microspheres by Suspension Copolymerization of Ethylene Glycol Dimethacrylate with Hydrophilic Monomers

YASUJI OHTSUKA, HARUMA KAWAGUCHI, and TAKUYA YAMAMOTO, *Department of Applied Chemistry, Faculty of Science and Technology, Keio University, 3-14-1, Hiyoshi, Kohoku-ku, Yokohama 223, Japan*

## Synopsis

A study was made of suspension copolymerization of ethylene glycol dimethacrylate (EDMA) with some hydrophilic monomers ( $M_2$ ) to prepare gel particles having a large number and various kind of functional groups on their surface. Delayed charge of  $M_2$  to partially prepolymerized EDMA suspension resulted in the formation of favorable particles. The polymerization leveled off despite an appreciable amount of remaining  $M_2$  in the aqueous phase, and the amount of copolymerized  $M_2$  and the fraction of on-surface  $M_2$  units depended significantly on the kind of  $M_2$  as well as the mode of  $M_2$  charge. These dependences were explained in terms of the partition coefficient of  $M_2$  between EDMA and water and the monomer reactivity ratio.

## INTRODUCTION

Polymer-microspheres having their functional groups densely in the surface layer bound to crosslinked core are expected to be capable of functioning similarly to gel particles having macroreticular structure as a specific adsorbent, a chromatographic resin, etc. In the previous study<sup>1</sup> some gel particles having a large amount of carboxyl groups in their surface layer were prepared by suspension copolymerization of diallyl phthalate (DAP) with carboxylic monomers, and the characteristics of the resulting particles were investigated. It was found that the copolymerization leveled off, although an appreciable amount of carboxylic monomer remained in the aqueous phase, and that the mode of monomer charge was the most important factor determining the amount of carboxylic monomer units bound to the particles and those existing in the surface layer.

In this study ethylene glycol dimethacrylate (EDMA), a more reactive crosslinkable monomer than DAP, was used in place of DAP and copolymerized with various hydrophilic monomers as well as carboxylic monomers to prepare gel particles having different kind of functional groups in their surface layer. The dependence of the characteristics of the copolymer particles on the reactivity of crosslinkable monomers and hydrophilic comonomers and on the reaction conditions was investigated. Some principles to design desirable particles will be summarized in the later section in this paper.

## EXPERIMENTAL

### Materials

Ethylene glycol dimethacrylate (EDMA) was distilled under reduced pressure. Hydrophilic comonomers ( $M_2$ ) used in this study were acrylic acid (AAc), methacrylic acid (MAc), sodium styrenesulfonate (SSStS), sodium 2-sulfoethyl methacrylate (SSEM), 4-vinylpyridine (VP), and 2-(dimethylamino)-ethyl methacrylate (DMAM). AAc, MAc, VP, and DMAM were distilled under reduced pressure. SSStS was reprecipitated from water with ethanol. All the chemicals mentioned above were obtained from Wako Pure Chemicals Co. SSEM was prepared by neutralizing hydrogen 2-sulfoethyl methacrylate (Polyscience, Inc.) with NaOH at a temperature lower than 10°C, followed by treating it with hydrous  $ZrO(OH)_2$  and then with activated charcoal. Benzoyl peroxide (BPO) was reprecipitated from chloroform with methanol. Poly(vinyl alcohol) (PVA) (Wako Pure Chemicals Co.; the degree of polymerization is 500 and the degree of saponification is 91.6%) was used as a dispersion stabilizer.

### Copolymerization

10 g of EDMA was dispersed in 200 g of an aqueous PVA solution in a four-necked flask and prepolymerized by BPO at 70°C under nitrogen. After a certain duration of prepolymerization, either of the  $M_2$ 's (1–5 g) was charged to the EDMA suspension to copolymerize. The polymerizations were continued for 24 h unless otherwise noted.

### Characterization

The resulting suspensions were filtered and the particles and supernatant were titrated by the same methods employed in the previous study<sup>1</sup> to determine the amount of  $M_2$  units in the particle surface layer ( $C_s$ ) and the amount of  $M_2$  units in the aqueous phase ( $C_w$ ), respectively. The total amount of  $M_2$  units bound to the particles ( $C_p$ ) was calculated by subtracting  $C_w$  from the amount of charged  $M_2$  ( $C_t$ ). The reason why  $C_p$  cannot be determined directly by any titrations was mentioned in the previous paper.<sup>1</sup> The particle size was determined by light microscopy and the surface texture of the particles was observed by scanning electron microscopy (SEM). The apparent surface density of  $M_2$  units was calculated from the  $C_s$  and surface average diameter ( $D_s$ , which is equal to  $\Sigma D_i^3 N_i / \Sigma D_i^2 N_i$ , where  $N_i$  is the number of the particles with diameter  $D_i$ ).

### Partition Coefficient of $M_2$ between EDMA and Water

A certain amount of  $M_2$  was added into a test tube containing the same volume of EDMA and water. The content was shaken for 2 min and then kept standing at 70°C for 2 h. The amount of  $M_2$  equilibrated in each phase was determined by conductometric titration.

## RESULTS AND DISCUSSION

## Suspension Homopolymerization of EDMA

The polymerization at the standard recipe proceeded fast and the conversion went up to over 90% within 3 h. The particle size was inversely proportional to 1.6 powers of agitation rate, and this relation coincided with that for DAP system.<sup>1</sup> The particle size decreased with increasing amount of PVA in the PVA concentration range from 0.125% to 0.75%. This trend coincides with Hopff's result<sup>2</sup> rather than the Narkis's one<sup>3</sup> and is perhaps explained on the basis of the concentration range of PVA employed as mentioned in the previous paper.<sup>1</sup> The average diameter of poly(EDMA) particles was smaller by about two thirds than that of poly(DAP) particles. This would be attributed to the higher hydrophilicity of EDMA which results in the formation of wider surface of the particles, and/or to the faster reaction of EDMA which reduces the occasion for the particles to aggregate.

Dependence of the Particle Structure on the Mode of  $M_2$  Charge

First the influence of the mode of AAc charge on the structure of EDMA-AAc copolymer particles was investigated, and the results were compared with those of the DAP-AAc system. Figure 1 shows that the later charge of AAc into the partially prepolymerized DAP or EDMA suspension caused  $C_p/C_t$  and  $C_s/C_t$  to decrease. This is believed to occur because the higher conversion of DAP or EDMA depresses the diffusion of AAc from the aqueous phase into the particles. In DAP-AAc copolymerization, later charge of AAc was apt to result in flocculation and only the particles obtained from the copolymerization in which AAc was charged at an earlier stage were characterizable. In EDMA-AAc copoly-

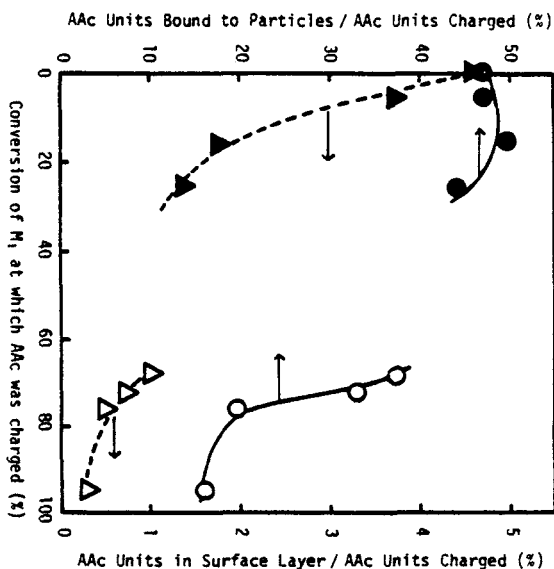


Fig. 1. Dependence of distribution of AAc units in copolymer suspension on conversion of cross-linkable monomer ( $M_1$ ) at which AAc was charged.  $M_1$ : (O, Δ) EDMA; (●, ▲) DAP. Copolymerization conditions: AAc/ $M_1$ /BPO/PVA/water = 5/10/0.2/1.0/200 (g) at 70°C.

merization, on the contrary, later charge of AAc made the reaction proceed smoothly and led to the formation of the particles having good appearance, although the reason for this difference is unknown at the present time. Due to the difference in the favorable timing for AAc charge, the conversion of cross-linkable monomers ( $M_1$ , EDMA or DAP) at which AAc was charged did not overlap each other in these two systems, as shown in Figure 1. Therefore, there was no other means of discussing the dependence of the particle structure on the kind of  $M_1$  but to compare their respective values extrapolated to the intermediate conversion range. The ratio of  $C_p$  to  $C_t$  for the EDMA-AAc system seems to be a little larger than that for the DAP-AAc system, assuming that AAc is charged at the same conversion of  $M_1$  in each copolymerization. This is attributed to the higher partition coefficient (PC) for AAc between EDMA and water (1.09, see Table I) compared with that between DAP and water (0.47) and perhaps to the larger surface area for EDMA-AAc particles than that for DAP-AAc particles because a wide surface gives more chance for AAc to diffuse from the aqueous phase to the particles.

The ratio of  $C_s$  to  $C_t$  for the EDMA-AAc system also seems to be larger than that for the DAP-AAc system. This would arise from the same reason as mentioned above, mainly from the higher ratio of the surface area to the volume of the EDMA-AAc particles compared with that of DAP-AAc particles.

The influence of the timing of AAc charge on the ratio of  $C_s$  to  $C_p$  in the DAP-AAc system is very different from that in the EDMA-AAc system. In the latter system the ratio decreased little with delaying AAc charge. On the other hand, the ratio in the DAP-AAc system decreased significantly as AAc was charged at a later stage. This is interpreted in terms of the density of cross-linkage and the monomer reactivity ratio. In the copolymerization of DAP ( $M_1$ ) with AAc ( $M_2$ ), AAc polymerizes preferentially as expected from the small  $r_1$  (0.043) and the large  $r_2$  (19.1). The resulting AAc unit-rich polymer chain is

TABLE I  
Relation among Partition Coefficient, Monomer Reactivity Ratio, and Apparent Surface Density of  $M_2$  Units on Copolymer Gel Particles

$M_1$	$M_2^a$	(g)	$r_1$	$r_2$	Partition <sup>b</sup> coefficient	Apparent surface density (unit/A <sup>2</sup> )
DAP <sup>c</sup>	AAc	5	0.044	19.1	0.47	15.1
	MAc	5	0.021	44.1	1.99	33
EDMA	AAc	1	0.87	0.87	1.09	0.4
		5				2.4
	MAc	1	1.24	0.79	4.76	2.4
		5				146
	SStS	5	0.29	1.73	0.14	0.04
	SSEM	3			0.48	4.18
	VP(free)	5	0.97	0.85	1.69	7.1
	VP-HCl	5			0.06	1.3
DMAM(free)	5	1.37	0.69	3.35	0.01	
DMAM-HCl	5			0.00	0.00	

<sup>a</sup>  $M_2$  was charged to 1 h prepolymerized  $M_1$  suspension.  $M_2/M_1/BPO/PVA/water = 5/10/0.2/1.0/200$  (g).

<sup>b</sup>  $[M_2]$  in  $M_1/[M_2]$  in water at 70°C.

<sup>c</sup> From Ref. 1, in which copolymerization was carried out at 80°C.

possible to phase-separate from the DAP solution in the particle, and, if the crosslinkage is less developed, that is, if the conversion of DAP is low enough, the hydrophilic polymer chain will diffuse back from the interior to the surface layer of the particle. As a result of this, the  $C_s/C_p$  is large when AAC is charged to less prepolymerized DAP suspension. A later charge of AAC to more cross-linked DAP particles would cause depression of the diffusion of AAC unit-rich polymer chain and decrease  $C_s/C_p$  remarkably. In EDMA–AAC copolymerization, on the other hand, their  $r_1$  and  $r_2$  values, relatively close to unity, and the required delayed charge of AAC make such phase separation hard to occur.

Two other  $M_2$ 's having acidic groups, MAc and SStS, and a cationic  $M_2$ , DMAM, were copolymerized with EDMA at different timings of  $M_2$  charge. The results are shown in Figures 2, 3, and 4. It is found from Figures 2 and 3 that both ratios,  $C_p/C_t$  and  $C_s/C_p$ , decrease with delaying charge of  $M_2$ 's in the EDMA–MAc and EDMA–DMAM systems. The decrease in  $C_p/C_t$  must result from the depressed diffusion of  $M_2$  from the aqueous phase into the particles due to a lesser amount of remaining  $M_1$ , a solvent for  $M_2$ , in the particles. The decrease in  $C_s/C_p$  is attributed to the above-mentioned phase separation, which would take place more or less in every copolymerization. It is noteworthy to mention that the timing of  $M_2$  charge did not affect the particle size and, therefore, the dependence of  $C_s/C_p$  on the timing of the  $M_2$  charge is not attributed to a particle size effect.

Contrary to the cases for weakly acidic  $M_2$ , the  $C_p$  was small and  $C_s/C_p$  did not change but was kept to be more than 0.96 for the EDMA–SStS system. The strong polarity of SStS must be responsible not only for the small  $C_p$  but also for negligible permeation of SStS to the interior of the particles, that is, for the  $C_s/C_p \sim 1$ . The relation between the property of  $M_2$  and the characteristics of the copolymer particles will be discussed in the following section with reference to the monomer reactivity ratio and PC of  $M_2$  between  $M_1$  and water.

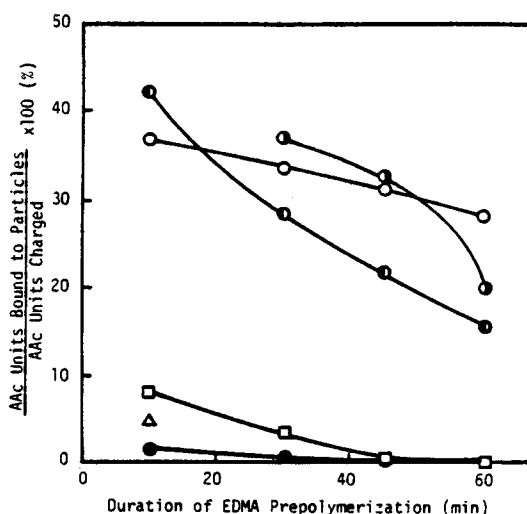


Fig. 2. Dependence of fraction of  $M_2$  units bound to particles on duration of prepolymerization of EDMA: (○) MAc (1 g); (●) AAC (5 g); (○) AAC (1 g); (□) DMAM (1 g); (△) SSEM (3 g); (●) SStS (5 g).

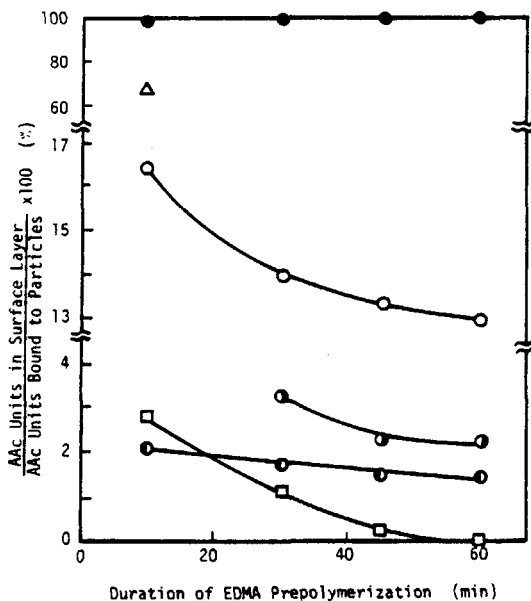


Fig. 3. Dependence of fraction of  $M_2$  units existing in surface layer of particles on duration of prepolymerization of EDMA. Symbols are the same as those used in Figure 2.

### Influence of the Neutralization of Weakly Basic $M_2$ 's on Their Distribution in the Suspension

Free or neutralized VP and DMAM were suspension-copolymerized with EDMA, and the results are summarized in Table II. In EDMA-VP copolymerization, neutralization of VP forced VP to leave in the aqueous phase and resulted in the formation of the particles having a lesser amount of on-surface

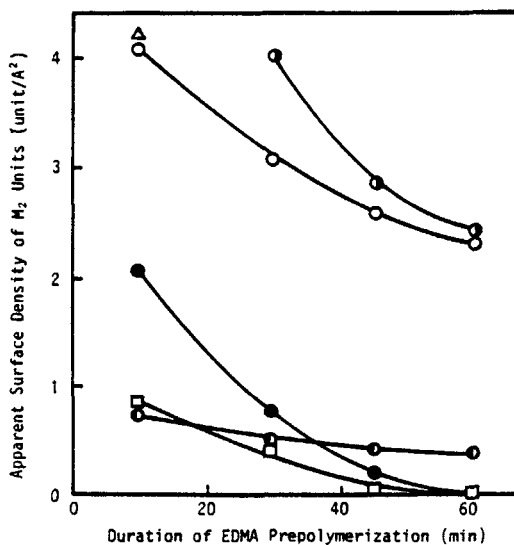


Fig. 4. Dependence of apparent surface density of  $M_2$  units on duration of prepolymerization of EDMA. Symbols are the same as those used in Figure 2.

TABLE II  
Preparation of Copolymer Particles Using EDMA and Cationic Monomers in Different Forms

$M_2^a$	Form	$D_s$ ( $\mu$ )	Total conversion (%)	$C_p/C_t$ (%)	$C_s/C_t$ (%)	Apparent surface density (unit/A <sup>2</sup> )
VP	Free	40.6	98.0	100.0	3.98	7.1
	Neutralized <sup>b</sup>	39.4	62.1	5.73	0.55	1.3
DMAM	Free	51.2	51.6	0.02	0.004	0.01
	Neutralized <sup>b</sup>	51.1	50.3	0.00	0.000	0.00

<sup>a</sup>  $M_2$  was charged to the 1-h prepolymerized EDMA suspension.  $M_2$ /EDMA/BPO/PVA/water = 5/10/0.2/1.0/200 (g).

<sup>b</sup> With HCl.

VP units. Behavior of DMAM in the copolymerization with EDMA was somewhat incomprehensive. The affinity of DMAM to EDMA is estimated to be comparable to that of VP judging from the PC's in Table I. Nevertheless, an extremely slight amount of DMAM copolymerized with EDMA even in its free form. This was found to be due to the low conversion of DMAM and EDMA. It is speculated that amino group in DMAM forms a redox system with BPO, and the radicals produced by the redox reaction at 70°C would be exhausted rapidly. Matsumoto attributed the unsuccessful aqueous polymerization of DMAM by potassium persulfate to such redox mechanism.<sup>4</sup>

#### Determinant for the Distribution of $M_2$ Units in Copolymer Suspension

As mentioned above,  $C_p$ ,  $C_s$ , and the ratio are significantly dependent on the kind of monomers. In this section the factors determining the apparent surface density of  $M_2$  units (SD), which is the most important characteristic for the gel particles, are discussed. The SD's for the particles prepared by various suspension copolymerizations are presented in Table I with the PC and monomer reactivity ratio for the examined monomer pairs. The PC's of some  $M_2$ 's between EDMA and water were found to be very close to those of  $M_2$ 's between methyl methacrylate and water<sup>5</sup> and, as predicted, larger than those between DAP and water.

It is expected that the particles having a large SD would be obtained by using an  $M_2$  which is easily diffusible into partially prepolymerized EDMA particles and rather homopolymerizable to diffuse back, by phase separation, to the surface layer from the interior of the particle, which is the main reaction locus.  $M_2$  should have a high PC and small  $r_1$  and large  $r_2$  to satisfy the above-mentioned conditions. It is found from Table I that the most fitting combination is DAP and MAC, and, in fact, the particles having a large SD were obtained from the copolymerization of DAP with MAC.

It is obvious from the values of  $r_1$  and  $r_2$  in Table I that, in contrast to DAP, EDMA tends to copolymerize randomly with each  $M_2$ . SStS might be an exceptional one which has a relatively small  $r_1$  and large  $r_2$ . But EDMA-SStS copolymerization did not form the particles having a large SD. This would arise from the small PC, as mentioned in the previous section. Not only this case but also most other cases indicated that PC is the predominant factor determining the SD of the particles prepared by the copolymerization with EDMA. Co-

polymer particles containing VP(free), AAc, and MAc, which have relatively large PC's, had larger SD's and, on the other hand, particles containing VP-HCl, which has a small PC, had a smaller SD. In Figures 2 and 4 the respective plots for EDMA-SSEM copolymer particles are presented. The larger  $C_p/C_t$  and the larger SD for SSEM-containing particles compared with those for SStS-containing particles are also interpreted by the difference in the PC's between two strongly acidic  $M_2$ 's. The unexpected behavior of DMAM(free), whose PC and reactivity ratio are close to those of MAc, was attributed to the inhibited polymerization, as mentioned in the previous section.

It must be noteworthy to mention an exceptional case in which higher affinity of  $M_2$  to  $M_1$  and lower copolymerizability do not lead to the formation of  $M_2$  unit-rich surface layer. According to a study on surface-modified gel plates,<sup>6</sup> which were prepared by immersing the prepolymer gel plate of diethylene glycol

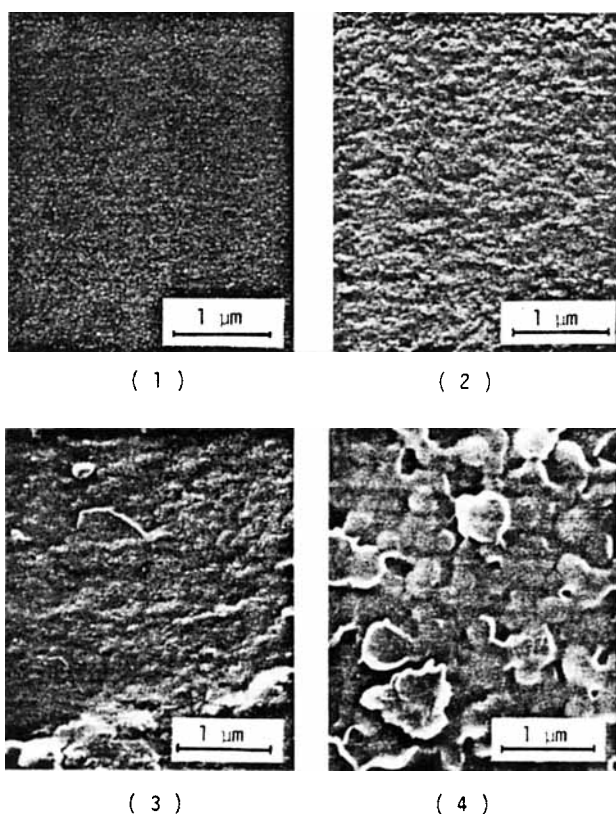


Fig. 5. SEM pictures of particle surface:

$M_2$	(g)	Duration of prepolymerization of EDMA (min)
(1) AAc	1	10
(2) SStS	5	10
(3) VP(free)	5	60
(4) MAc	5	60



TABLE III  
Relation between Surface Texture of Gel Particles and Apparent Surface Density of  $M_2$  Units

Surface texture	$M_1^a$	$M_2$	(g)	Duration of prepolymerization (min)	Apparent surface density (unit/A <sup>2</sup> )
Smooth	DAP	—			—
	EDMA	—			—
		AAc	1	10	0.75
Finely rugged	DAP	SStS	5	60	0.04
		MAc	5	240	1.7
	EDMA	VP-HCl	5	60	1.3
		SStS	5	10	2.09
		AAc	5	60	2.4
		MAc	1	10	4.08
Wrinkling	DAP	MAc	5	0	70
				60	33
	EDMA	VP(free)	5	60	7.1
		MAc	5	60	146

<sup>a</sup>  $M_1$ , 10 g.

bis(allyl carbonate) (CR-39) to an aqueous solution of  $M_2$ , followed by *in situ* copolymerization, SStS has slightly higher affinity to CR-39 than SSEM, but the SD of SStS on the gel plate is smaller than that of SSEM. As the preparation of the copolymer gel plate of SStS accompanied a weight loss of the plate, the above-mentioned result was explained by some release of SStS unit-rich polymer chain from the surface to the aqueous phase.

In the present case, the crosslinkage is more developed than in the gel plate cited, and copolymerizability of  $M_2$  with EDMA is higher than that with CR-39. Under such conditions, PC seems to be the predominant factor determining SD.

### Observation of Surface Structure of Copolymer Gel Particles

It was reported in the previous paper<sup>1</sup> that the particle having a large SD has a rough surface while the one having a small SD has a smooth surface. This relation was recognized not only in the copolymer particles but also in some copolymer gel plates.<sup>7</sup> The surface of various particles was observed by SEM and the representative pictures are shown in Figure 5. The surface texture is classified into three groups with respect to the smoothness or roughness of the surface. Table III confirmed the above-mentioned relation between SD and surface structure. The fourth picture in Figure 5 presents the surface texture of a particle prepared by the copolymerization in which 5 g of MAc was charged in 1-h-prepolymerized EDMA suspension. Such structure has never been seen even in any DAP- $M_2$  copolymerization systems as well as in other EDMA- $M_2$  systems. The SD of this particle was extremely large. These facts may imply the possibility that some EDMA radicals occasionally localized on the particle surface became nuclei of microspheres, seen in the picture, which were mainly composed of MAc and loosely crosslinked. In this sense the situation of this copolymerization may resemble that of copolymerization to prepare macroreticular particles.<sup>8</sup>

## CONCLUSIONS

Ethylene glycol dimethacrylate (EDMA) was copolymerized with some hydrophilic monomers ( $M_2$ ) in suspension to prepare functional gel particles. Acrylic acid, methacrylic acid, sodium styrenesulfonate, sodium 2-sulfoethyl methacrylate, 4-vinylpyridine, and 2-(dimethylamino)-ethyl methacrylate were charged delayedly to the partially prepolymerized EDMA suspension. In most copolymerizations the reaction leveled off, although an appreciable amount of  $M_2$  remained in the aqueous phase. Earlier charge of  $M_2$  led to the increases in the amount of  $M_2$  units bound to the particles and in the fraction of  $M_2$  units exposed on the particle surface.

The apparent surface density of  $M_2$  units on EDMA- $M_2$  copolymer particles was generally smaller than that on diallyl phthalate- $M_2$  particles. This was attributed to the difference in the favorable timing of  $M_2$  charge and in copolymerizability between two systems. Summarized results confirmed the principle that the gel particles having a high surface density of functional groups can be prepared by the copolymerization of crosslinkable monomers with hydrophilic monomers, which have high affinity but relatively low copolymerizability with crosslinkable monomers.

## References

1. Y. Ohtsuka, H. Kawaguchi, and T. Hamasaki, *J. Appl. Polym. Sci.*, to appear.
2. Von H. Hopff, H. Lussi, and P. Gerspacher, *Macromol. Chem.*, **78**, 24 (1964).
3. M. Narkis, *J. Appl. Polym. Sci.*, **23**, 2043 (1979).
4. T. Matsumoto, private communication.
5. T. Matsumoto and M. Shimada, *Kobunshikagaku*, **22**, 172 (1965).
6. N. Kaneko and Y. Ohtsuka, *J. Appl. Polym. Sci.*, to appear.
7. Y. Ohtsuka, N. Kaneko, and F. Takami, *J. Appl. Polym. Sci.*, **26**, 2423 (1981).
8. K. A. Kun and R. Kunin, *J. Polym. Sci.*, *A-1*, **6**, 2689 (1968).

Received December 23, 1981

Accepted February 26, 1982