

Coating Water-Swellable Polymer Latexes by Interfacial Polymerization

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SYNOPSIS

Two techniques of coating water-swellable polymer latexes (hydrogels) with an inorganic or organic layer were developed, based on interfacial polymerization. The hydrogel latexes were prepared by inverse suspension polymerization. The first kind of interfacial polymerization is hydrolysis and polycondensation of tetraethyl orthosilicate (TEOS) or 3-(trimethoxysilyl)propylmethacrylate (TMS-PMA) on the surface of hydrogel latexes. The hydrochloric acid, which is the catalyst for this reaction, was previously loaded into the hydrogel latexes. The HCl-containing hydrogel latexes were then suspended in an organic solution of TEOS or TMS-PMA. The hydrolysis and condensation occur only at the surface of each hydrogel particle and the generated SiO₂ or SiO(PMA) network covers the hydrogel latexes. The second interfacial polymerization is polymerization of methylenedi-*p*-phenyl diisocyanate (MDI) and triethylene glycol (TEG) on the surface of hydrogel latexes. TEG was deposited on the hydrogel by suspending the hydrogel powder in a tetrahydrofuran (THF) solution of TEG and evaporating the THF. The TEG-deposited hydrogel powder was then suspended in an organic solution containing both MDI and the catalyst dibutyltin dilaurate (DBTL). The MDI and DBTL molecules react with the TEG molecules only at the surface of the hydrogel particles, and the polyurethane P(MDI-TEG) thus formed wraps the particles. Based on these two coating procedures, three kinds of materials were obtained: SiO₂ coated hydrogels, SiO-(PMA) coated hydrogels and P(MDI-TEG) coated hydrogels. Soft polyether brushes were grafted to the SiO-(PAM) coated latexes. The P(MDI-TEG) coated hydrogels were used as reservoirs for β -hydroethyltheophylline (β -HETP), and the release of the latter molecules from the coated hydrogels was investigated.

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INTRODUCTION

Hydrogels are water-swellable polymer networks possessing the cohesive properties of solids and the diffusive transport properties of liquids.¹ The capacity of highly water-swellable polymer gels to retain large amounts of water makes them useful in a variety of applications. Because all biological systems are water based, and most are ionized aqueous gels, hydrogels have been employed as reservoirs for drug release,² and used for the microencapsulation of enzymes and cells in order to protect them.³

In this article the emphasis is on the surface coating of hydrogel particles with an inorganic or

organic layer by interfacial polymerization. Two methods were developed to carry out the interfacial polymerization. In the first, a hydrogel powder that has already absorbed a sufficient amount of an aqueous solution of HCl was suspended with stirring in an organic medium (toluene) that contains tetraethyl orthosilicate (TEOS) or 3-(trimethoxysilyl)propyl methacrylate (TMS-PMA). The hydrolysis and polycondensation⁴ of the latter molecules is catalyzed by the HCl present on the surface of the hydrogel latexes because the aqueous solution of HCl cannot be extracted by toluene. In the second method a hydrogel powder, on which a low molecular weight of polyethylene glycol (PEG, such as triethylene glycol, TEG) was uniformly deposited, was suspended with stirring in an organic medium (toluene) containing methylene-*p*-diphenyl diisocyanate (MDI) and the catalyst dibutyltin dilaurate

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(DBTL). The reaction between MDI and PEG (which can occur only at the surface of the hydrogel latexes because PEG does not dissolve in the organic medium at the ambient reaction temperature employed) leads to a surface layer of polyurethane (PU).

The coating of hydrogel latexes is useful in several respects. $\text{Ti}(\text{OEt})_4$, $\text{Zr}(\text{OC}_4\text{H}_9)_4$, and $\text{Pb}(\text{NO}_3)_2$ are precursors for piezoelectric materials. Their hydrolysis and condensation on the surface of hydrogel particles results in an inorganic layer, such as the lead zirconate titanate, wrapping the hydrogel core. Thin-walled, hollow ceramic spheres^{5,6} are expected to form when the hydrogel core is removed by heating at high temperatures. The hydrolysis and polycondensation of TMS-PMA on the surface of hydrogel particles generates a SiO-(PMA) surface network. A variety of polymer chains can be grafted to the pendant PMA groups of this network. A composite containing hydrogel particles immersed in a continuous polymer network can thus be obtained. Such a composite may become a candidate for biocatalytic membranes.⁷ Polyanion networks possess a much higher capacity to retain an aqueous solution containing a drug than any other nonionic hydrophilic matrix. Polyanions can, however, exhibit biological activities⁸ by themselves. To avoid the undesired effects caused by the direct contact of polyanions with the bioenvironment, it is suitable to coat the drug-loaded polyanionic hydrogel latexes with a PU layer. The PUs can acquire a variety of

physicochemical properties through the changes in their soft and hard segments as well as in their chain extenders.⁹

Five kinds of water-swellaible polymer latexes (Fig. 1) were synthesized by the inverse suspension polymerization method. The main goal of the present work was to develop techniques for the coating of the particles of the above hydrogels via interfacial polymerization. Three kinds of materials have been obtained (for abbreviations see Fig. 1): the inorganic-organic hybrid of SiO_2 coated P(NaSS-MBAM) and SiO_2 coated P(NaAMPS-MBAM) latexes; the grafted composites between SiO(PMA) coated P(AM-MBAM) or SiO(PMA) coated P(HEMA-MBAM) latexes and the poly[α -acryloyl poly(propylene glycol) oligomer]; the polyurethane P(MDI-TEG) coated polyanion hydrogels. In addition, the effect of the coating layer on the release of β -hydroxyethyl-theophylline (β -HETP, a medicine) from the P(NaSS-MBAM) hydrogel was investigated.

EXPERIMENTAL

Materials

Reagents

TEOS (98%), TMS-PMA (97%), poly(propylene glycol) (PPG) average M,W 725, acryloyl chloride

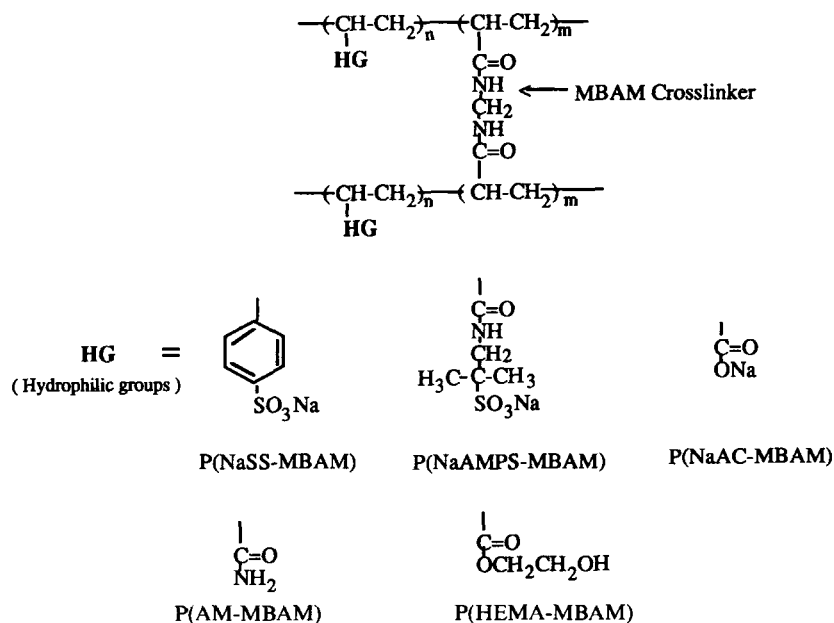


Figure 1 Water-swellaible polymers prepared by the inverse suspension polymerization.

(98%), TEG (98%), DBTL (98%) were purchased from Aldrich. MDI was purchased from Kodak and β -HETP from Sigma.

Water-Soluble Monomers

Sodium 4-styrenesulfonate (NaSS) (97%), (2-acrylamido-2-methyl-1-propanesulfonic acid (AMPS) (99%), acrylamide (AM) (99+T), *N,N'*-methylenebisacrylamide (MBAM) (99+%), 2-hydroxyethyl-methacrylate (HEMA), and acrylic acid (99%) were purchased from Aldrich. HEMA and acrylic acid were passed through an inhibitor removal column before use.

Water-Swellable Polymer Latexes

A representative preparation of P(NaAMPS-MBAM) was carried out as follows: AMPS (9.64 g, 46 mmol) and MBAM (1.54 g, 10 mmol) were dissolved in 30 mL water. A solution of 1.8 g NaOH in 5 mL water was added to the above solution with stirring. $K_2S_2O_8$ aqueous solution (3.5 mL, 1.57×10^{-2} g/mL) was introduced into the solution of monomers. The aqueous system (pH = 8) was dispersed with magnetic stirring into 25 mL toluene that contained 1.0 g of Span-80 as emulsifier. The inverse suspension was purged under N_2 and sealed. After polymerization for 24 h at 60–65°C with stirring, about 50 mL of tetrahydrofuran (THF) were introduced into the system to precipitate the P(NaAMPS-MBAM) latexes. The latexes were then washed several times with acetone. Thus, 11 g of white powder were obtained. Elemental analysis indicated that 1 g of P(NaAMPS-MBAM) contained 3.5 mmol of NaAMPS and 0.78 mmol of MBAM. In all the hydrogel latexes prepared (Fig. 1), the same molar ratio (as above) between the hydrophilic monomer and the crosslinking agent was employed.

Synthesis of α -Acryloyl PPG

PPG (14.5 g, 20 mmol) and triethylamine (2 g, 20 mmol) were dissolved in 40 mL THF. Acryloyl chloride (1.88 g, 20 mmol) was dropped slowly at room temperature into this solution with magnetic stirring. After this addition, the stirring was continued for 1 h, and the generated $Et_3N \cdot HCl$ was removed by passing the reaction mixture through a silica gel column. THF was then evaporated with flowing air to obtain the monosubstituted acryloyl PPG.

Coating Hydrogel Latexes via an Interfacial Sol-Gel Process

Preparation of P(NaAMPS-MBAM)/SiO₂ Core-Shell Composite

A water in oil emulsion was prepared by introducing 1 mL of HCl aqueous solution (1 N) with stirring in 20 mL toluene containing 1.0 g of Span-80. To this emulsion, 1.5 g of P(NaAMPS-MBAM) powder was added. The emulsion disappeared after the suspension was stirred for a few minutes because the droplets of HCl solution were absorbed by the P(NaAMPS-MBAM) particles. Then, TEOS (0.5 g), which is soluble in toluene, was added to this system. The hydrolysis and polycondensation of TEOS in this system was carried out, with stirring, at 40–50°C for 20 h. The SiO₂ coated powders were filtered and washed with THF in a Buchner funnel several times. P(NaSS-MBAM)/SiO₂ was prepared using a similar procedure.

Preparation of P(AM-MBAM)/SiO-(PMA) Core-Shell Composite

P(AM-MBAM) powder, 1.5 g, was added to the emulsion of 1.5 mL HCl (1 N) in 30 mL toluene

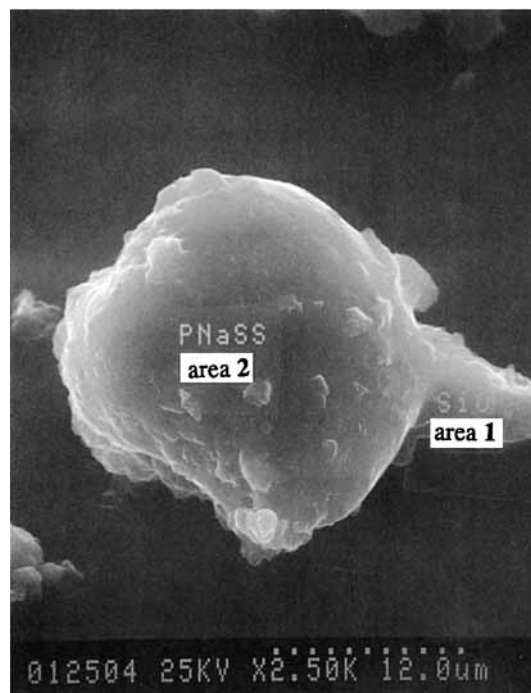


Figure 2 Scanning electron micrograph of SiO₂ coated P(NaSS-MBAM) latexes prepared by using 0.5 g of TEOS and 1.5 g of P(NaSS-MBAM).

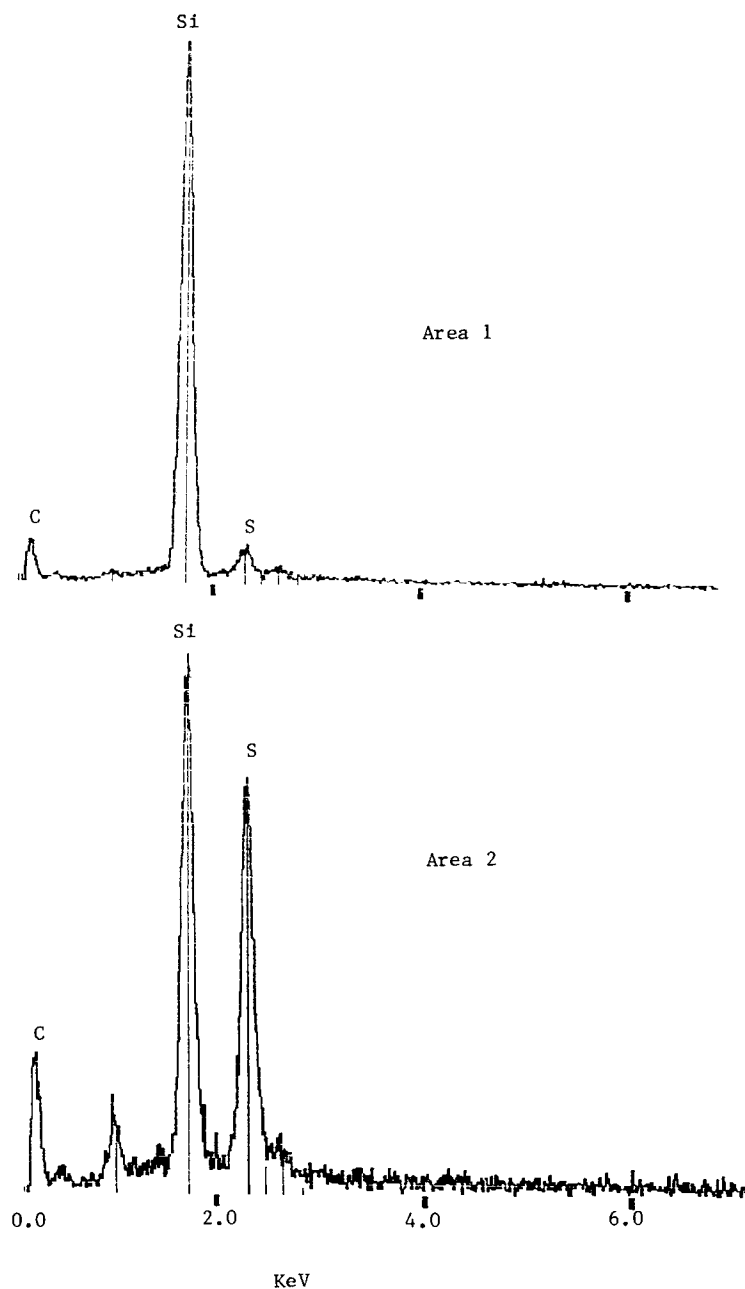


Figure 3 Energy dispersive spectra of the microareas 1 and 2 indicated in Figure 2.

containing 12 mg hydroquinone. After the dispersed aqueous solution was absorbed by P(AM-MBAM), 0.6 g of TMS-PMA was introduced into the system. The suspension was stirred overnight at 50–60°C. The obtained P(AM-MBAM)/SiO-(PMA) powders were filtered and washed with THF in a Buchner funnel. The P(HEMA-MBAM)/SiO-(PMA) was prepared using the same procedure.

Grafting Poly[α -acryloyl PPG] to P(AM-MBAM)/SiO-(PMA)

α -Acryloyl PPG, 1.5 g, and 50 mg of azobisisobutyronitrile (AIBN) were dissolved in 10 mL THF, and the solution was added to 0.5 g of P(AM-MBAM)/SiO-(PMA) in a 25 mL tube. Most of the THF was evaporated with an air flow, and the sys-

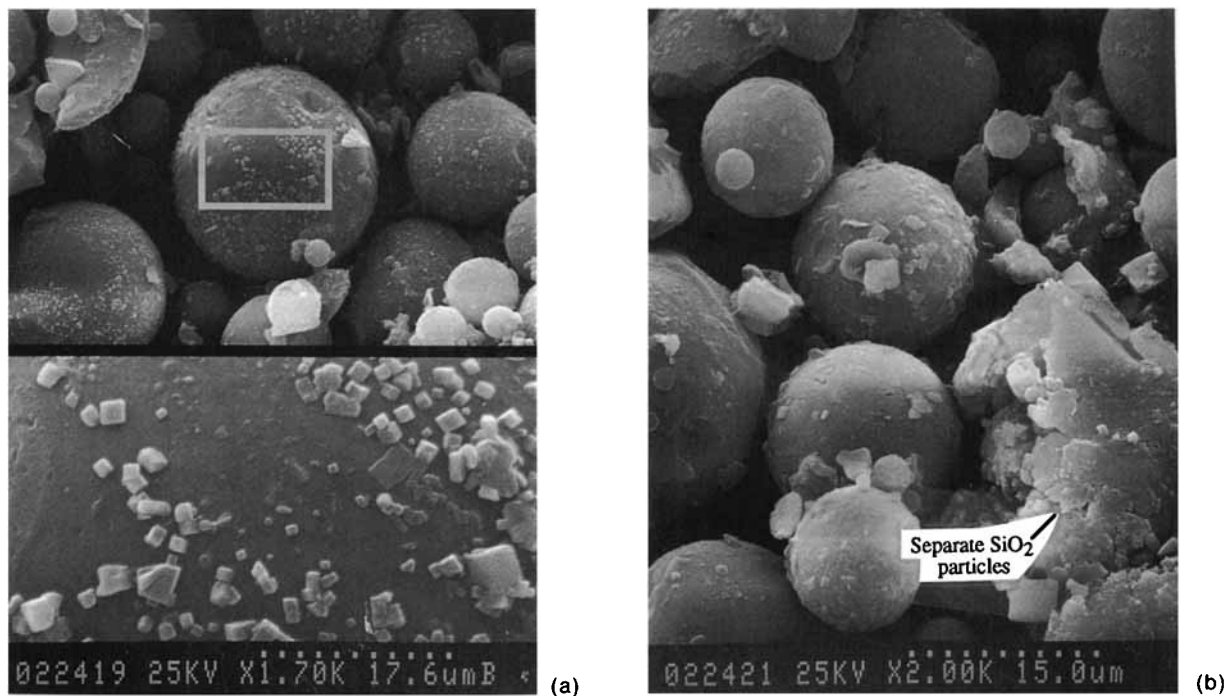


Figure 4 Scanning electron micrographs of SiO₂ coated P(NaAMPS-MBAM) latexes prepared by using different weight ratios of TEOS/P(NaSS-MBAM): (a) 0.16; (b) 0.33. (a) is almost free of separated SiO₂ particles; (b) contains separated SiO₂ particles detected by EDS.

tem was sealed under an N₂ atmosphere. Polymerization was carried out at 60°C overnight, and the product was purified by washing with THF. The grafting of poly[α -acryloyl PPG] to P(HEMA-MBAM)/SiO-(PMA) was achieved in the same manner.

Coating Hydrogel Latexes with PU

Loading β -HETP into P(NaSS-MBAM) Latexes

P(NaSS-MBAM) powder, 1.0 g, was introduced into an aqueous solution of 0.6 g β -HETP in 10 mL water. A water-swollen polymer gel was thus obtained. The

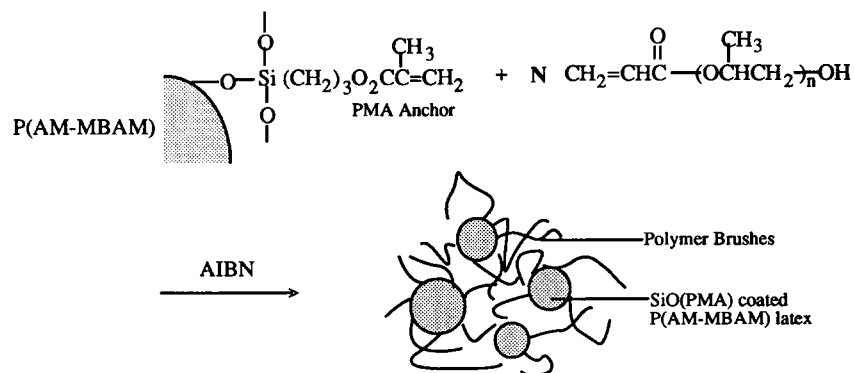


Figure 5 Preparation of the composite of SiO-(PMA) coated P(AM-MBAM) latexes and poly[α -acryloyl PPG].

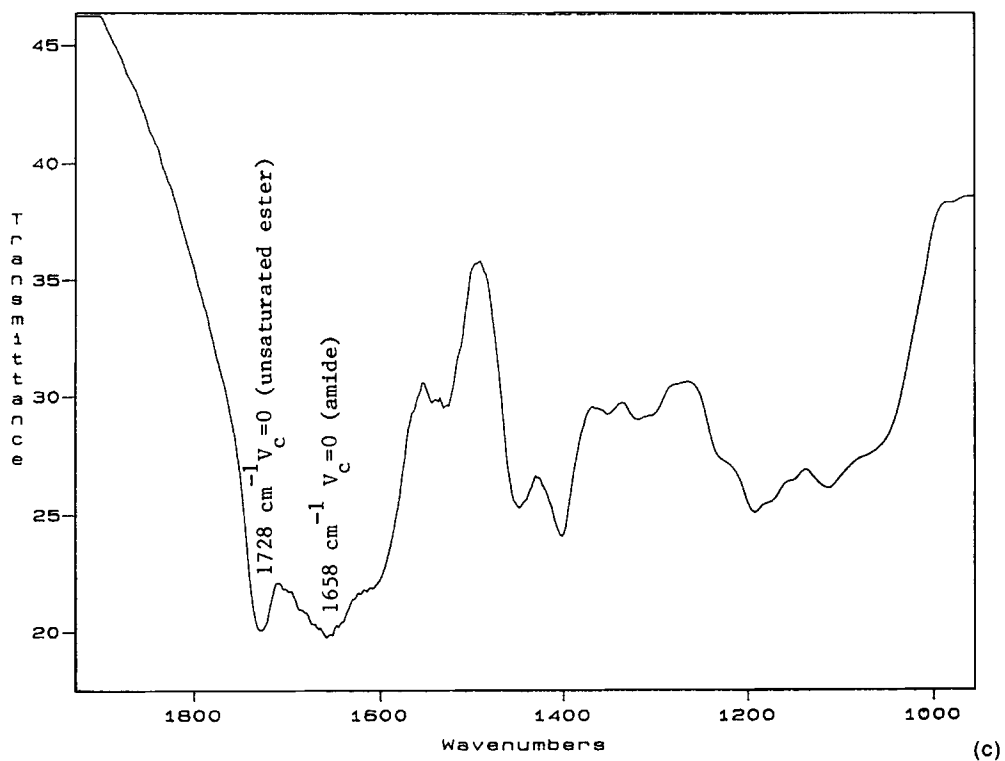
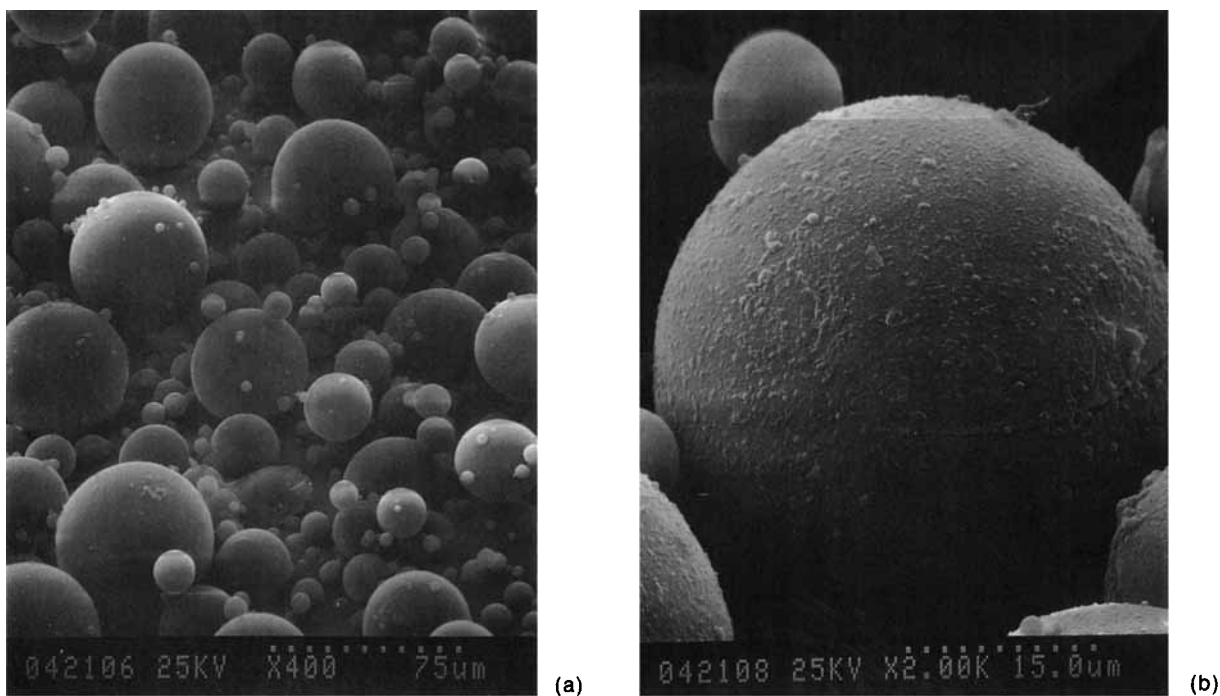


Figure 6 (a) Scanning electron micrograph of P(AM-MBAM) latexes; (b) scanning electron micrograph of the surface of a P(AM-MBAM) latex coated with SiO-(PMA); (c) FTIR spectrum of the SiO-(PMA) coated P(AM-MBAM) powder; (d) scanning electron micrograph of the composite of SiO-(PMA) coated P(AM-MBAM) latexes and grafted poly[α -acryloyl PPG].

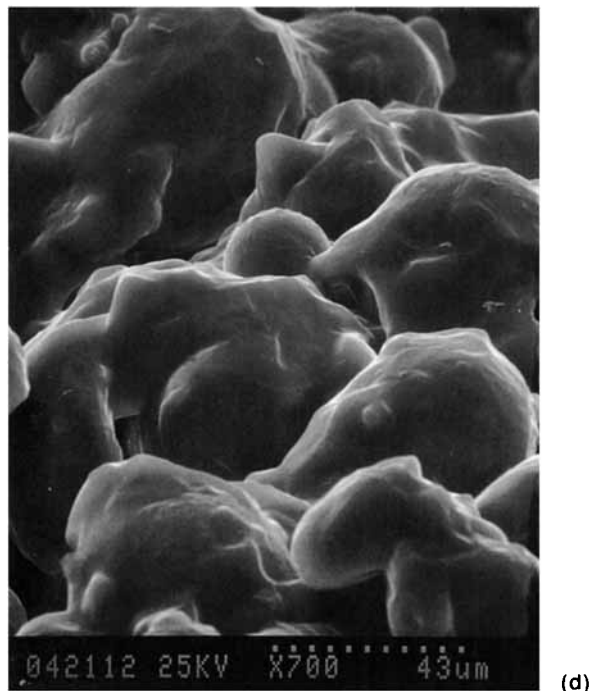


Figure 6 (Continued from previous page)

gel was placed in a fume hood overnight to evaporate most of the water, and the rest of the water was removed by vacuum drying at ambient temperature. The solid left was ground into a fine powder and washed with THF three times to dissolve the β -HETP molecules that did not penetrate into the polymer network. After drying, 1.4 g of β -HETP loaded P(NaSS-MBAM) powder was obtained. β -HETP was loaded in P(NaAMPS-MBAM) or in P(NaAC-MBAM) in the same manner.

Coating β -HETP Loaded P(NaSS-MBAM) Powder with Poly(MDI-TEG)

β -HETP loaded P(NaSS-MBAM) powder, 1.08 g, was introduced into 5 mL THF solution containing 0.21 g TEG and 0.002 g glycerol, and the solvent THF was evaporated with an air flow. The TEG deposited powder was then suspended overnight at room temperature in a 20 mL toluene solution containing 0.66 g of MDI and 0.01 g of DBTL. After filtering and washing with THF, 1.41 g of poly(MDI-TEG) coated P(NaSS-MBAM)/ β -HETP powder was obtained. The same method was used for coating the other two β -HETP loaded systems.

Test of Matrix Releasing

Poly(MDI-TEG) coated P(NaSS-MBAM) powder (0.04 g), which contained 1.26×10^{-2} g of β -HETP,

were introduced into 5 mL water. The concentration of β -HETP in water was determined using a high performance liquid chromatograph (ISCO-2350 pump/ISCO-V₄, detector, UV, 254 nm).

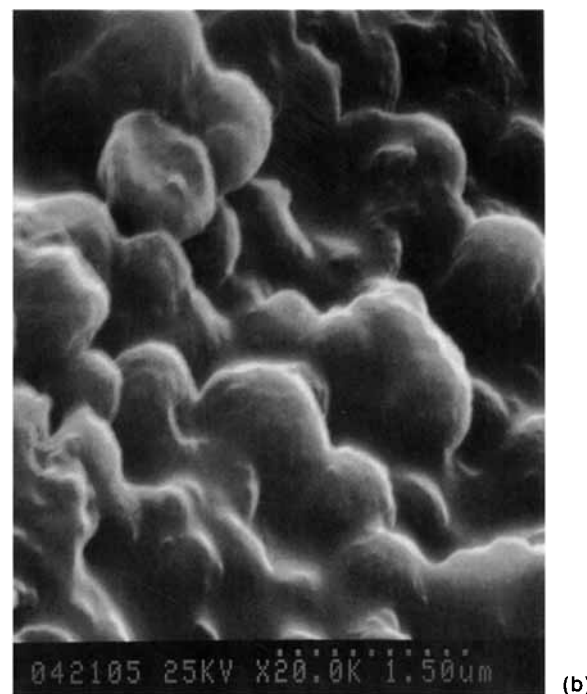
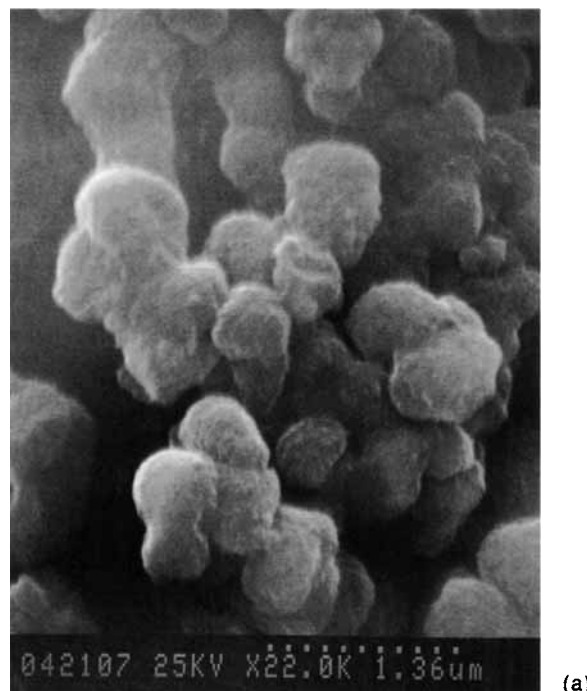


Figure 7 (a) Scanning electron micrograph of P(HEMA-MBAM) latexes; (b) scanning electron micrograph of the composite of SiO-(PMA) coated P(HEMA-MBAM) latexes and poly[α -acryloyl PPG].

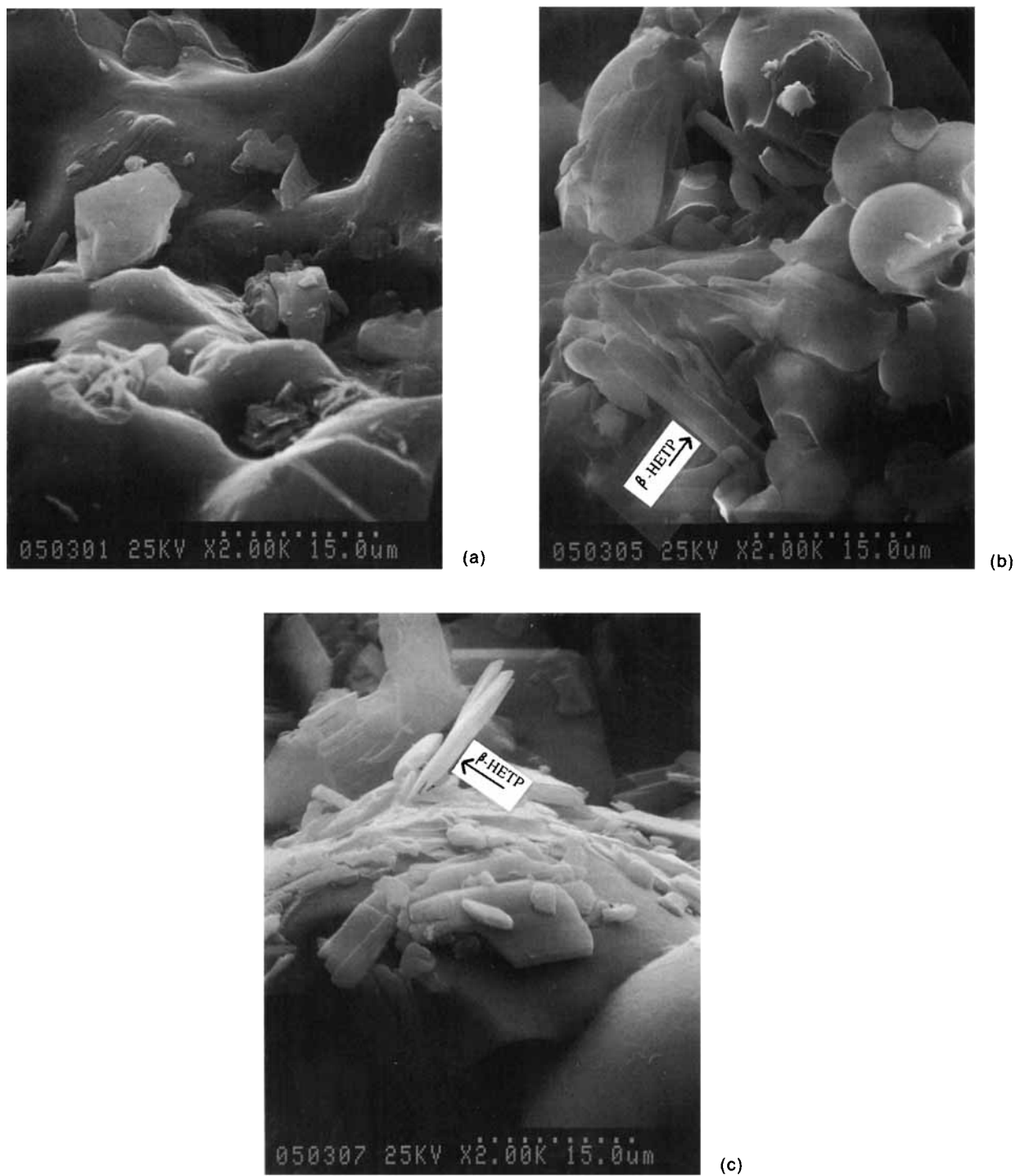


Figure 8 (a) Scanning electron micrograph of the β -HETP loaded P(NaSS-MBAM) network. (b) Scanning electron micrograph of the β -HETP loaded P(NaAMPS-MBAM) network; the surface wrapped β -HETP crystals are indicated by an arrow. (c) Scanning electron micrograph of the β -HETP loaded P(NaAC-MBAM) network; the surface attached β -HETP crystals are indicated by an arrow.

Instrumental Analysis

The SEM micrographs were obtained with a Hitachi S-800 Instrument, and the energy dispersive spectroscopy (EDS) was performed with PGT/TMIX field emission microscopy equipment. The infrared absorption spectra of the polymer composites were obtained with a Mattson Alpha Centauri FTIR instrument using a KBr grate.

RESULTS AND DISCUSSION

Coating Via Interfacial Sol-Gel Process

The technique used here for coating hydrogel latexes with a SiO_2 layer is, in fact, similar to the sol-gel method¹⁰ employed to prepare ceramic materials, via the hydrolysis and polycondensation of alkoxide precursors (TEOS or TMS-PMA in the present case), followed by aging and drying. It differs from the conventional one in that the hydrochloric aqueous solution (the acid catalyst needed for hydrolysis) is loaded into the water-swellaible matrixes of hydrogel latexes, which are suspended in an organic solution of TEOS or TMS-PMA. Consequently, the hydrolysis and polycondensation can occur only at the interface of the hydrogel latexes.

Two kinds of hydrogel latexes, P(NaSS-MBAM) and P(NaAMPS-MBAM), were coated with an SiO_2 layer by this interfacial sol-gel method. Figure 2 is a scanning electron micrograph of a spherical P(NaSS-MBAM) particle coated with an SiO_2 layer. EDS investigations (Fig. 3) indicate comparable peaks for Si and a much stronger peak for sulfur in the central than in the peripheral regions of the particle. This demonstrates that SiO_2 wrapped the hydrogel particle. The content of HCl (aq.) inside the hydrophilic particles as well as the amount of TEOS used must be controlled, because excess amounts of the two will also generate separate SiO_2 particles. To avoid the formation of separate SiO_2 particles, we found that the weight ratio of catalyst (1 N aqueous HCl) to P(NaSS-MBAM) or P(NaAMPS-MBAM) should be around unity. To uniformly distribute such a small amount of HCl (aq.) into the highly water-swellaible polymer latexes, an inverse emulsion of HCl (aq.) in toluene was first prepared and the P(NaSS-MBAM) powder was introduced into the emulsion. The effect of different weight ratios of TEOS to P(NaSS-MBAM) is demonstrated in Figure 4, which shows that for a ratio of 0.16 [Fig. 4(a)], the fraction of separate SiO_2 particles is small, while for a ratio of 0.33 [Fig. 4(b)], the fraction is much larger.

The sol-gel interfacial coating can be used to graft polymer brushes to the coated particles when a functional precursor, such as TMS-PMA, is used to generate a surface network of $\text{SiO}-(\text{PMA})$ (Fig. 5). Two kinds of hydrogel latexes, P(AM-MBAM) [Fig. 6(a)] and P(HEMA-MBAM) [Fig. 7(a)] were employed as substrates. Figure 6(b) shows the surface morphology of the $\text{SiO}-(\text{PMA})$ network coated P(AM-MBAM) particle. The FTIR spectrum [Fig. 6(c)] of the sample from Figure 6(b) indicates, via the absorption band at 1728 cm^{-1} (which represents the ν_{co} of α,β -unsaturated ester), the presence of the PMA groups. To prepare a composite of hydrogel latexes in an elastomeric polymer network, the $\text{SiO}-(\text{PMA})$ coated P(AM-MBAM) or P(HEMA-MBAM) were subjected to grafting with α -acryloyl PPG. The scanning electron micrographs [Figs. 6(d) and 7(b)] show the morphologies of the obtained composites. One can observe that isolated hydrogel latexes are dispersed in a continuous poly[α -acryloyl PPG] network.

Coating via PU Interfacial Polymerization

The PUs prepared via the polymerization of PEG containing chain extenders with various diisocyanates are important biomedical materials. It is worth

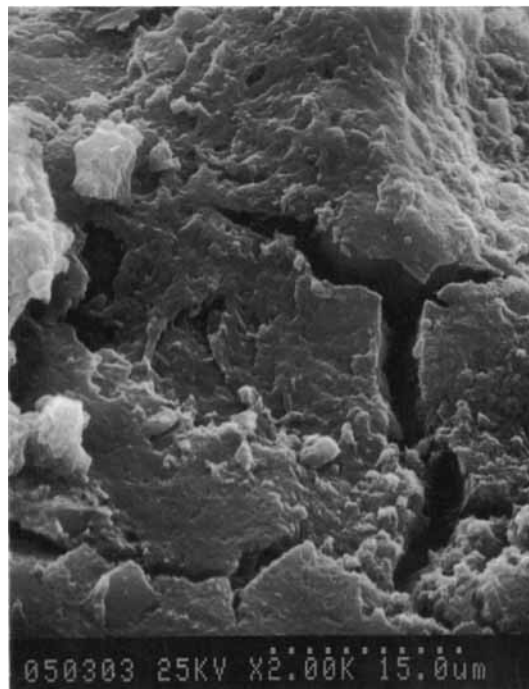


Figure 9 Scanning electron micrograph of the surface morphology of the β -HETP loaded P(NaSS-MBAM) coated with poly(MDI-TEG).

noting that the very different solubilities of PEG and diisocyanates in some low polar organic solvents (such as toluene, cyclohexane, isooctane) provide the possibility to coat hydrophilic latexes with a PU layer. PEG molecules can be deposited on the surface

of latexes by their dissolution in a solvent (THF) containing the latexes followed by the vaporization of the solvent. The suspension of the PEG-deposited latexes in a low polar organic medium containing a diisocyanate and a suitable catalyst (such as DBTL)

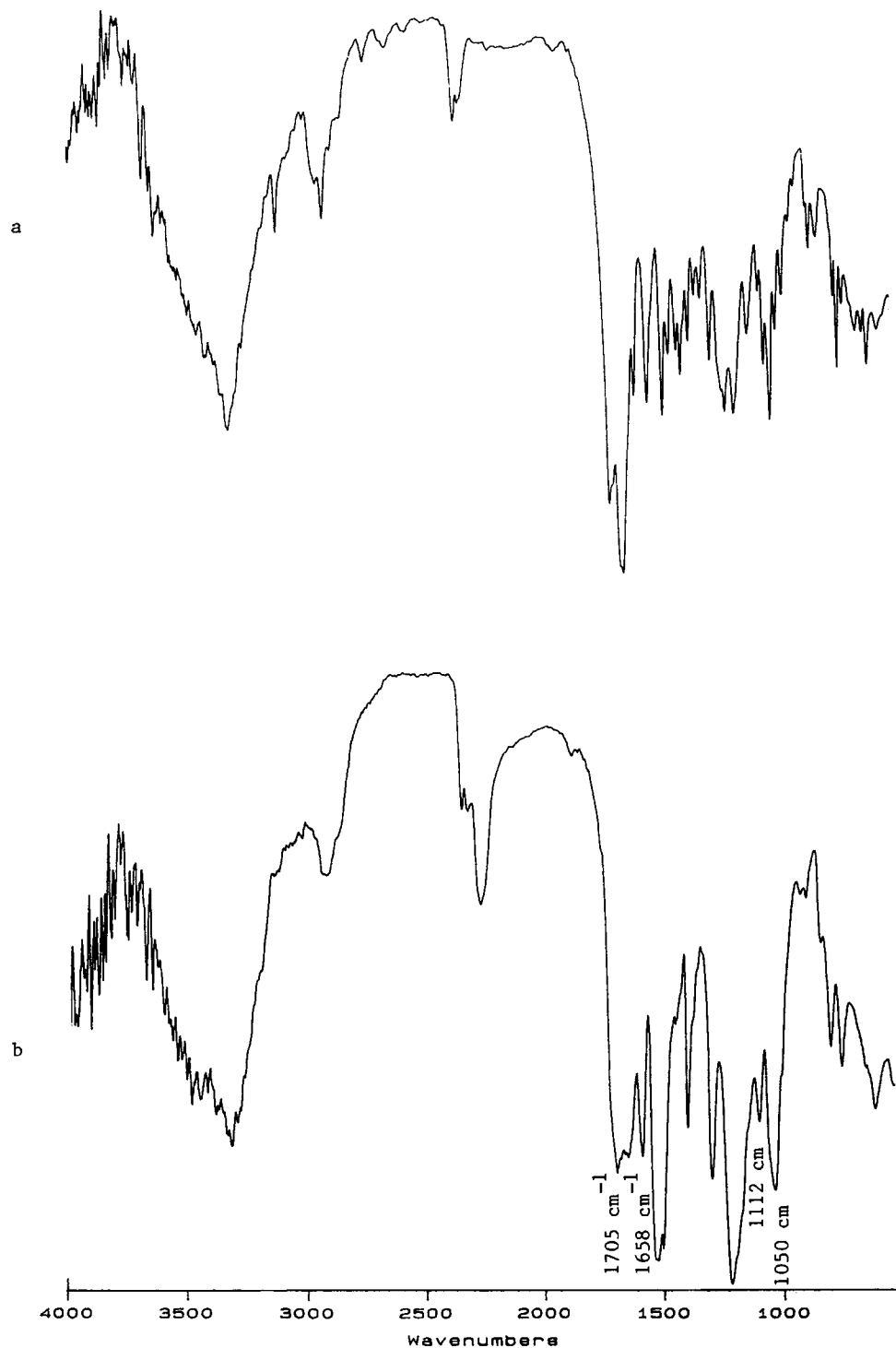


Figure 10 (a) FTIR spectrum of the β -HETP loaded P(NaSS-MBAM); (b) FTIR spectrum of the β -HETP loaded P(NaSS-MBAM) coated with poly(MDI-TEG).

can achieve, at room temperature, a coating layer of PU on the latexes.

The polyanion networks, P(NaSS-MBAM), P(NaAMPS-MBAM), or P(NaAC-MBAM), possess much higher capacities to absorb aqueous solution than the nonionic hydrophilic ones. When the water molecules are evaporated, the solute is retained within the polymer matrix, and a delivery system is generated. However, the anionic groups of these polymers can exhibit biological effects by themselves, which can be avoided by coating them with a biologically inert hydrophilic layer. β -HETP was selected as a biological agent, and the PU prepared from MDI and TEG was selected as the outside coating layer. The delivery system was prepared as follows. 1) β -HETP was loaded into the above polyanion powder by impregnation, and the obtained drug carrier was washed with THF, which is a solvent for β -HETP but not for the polymer matrix, in order to eliminate the drug present on the surface of the polymer. The content of β -HETP based on elemental analysis is: 0.41 g/g of polymer when P(NaSS-MBAM) was employed, 0.37 g/g when P(NaPMS-MBAM) was employed, and 0.36 g/g when P(NaAC-MBAM) was employed. The SEM investigations showed that β -HETP was more uniformly distributed inside the P(NaSS-MBAM) than inside the other two-hydrogels [Fig. 8(a-c)]. 2) TEG was deposited on the surface of β -HETP-loaded P(NaSS-MBAM) particles, and the coating via PU generation was carried out by stirring the TEG loaded particles in a toluene solution of MDI and (the catalyst) DBTL. The advantage of this coating process is that the reaction occurs at room temper-

ature. It will, therefore, prevent the surface deposited TEG to dissolve in the liquid phase and thus the damage of the loaded drug. Figure 9 shows a rough poly(MDI-TEG) layer [compared to Fig. 8(a)] on the surface of the β -HETP-loaded P(NaSS-MBAM) particle. The thickness of the coating layer could not be determined from the SEM picture because the spherical shape of P(NaSS-MBAM) was deformed after the loading with β -HETP. The amount of coated poly(MDI-TEG), however, could be evaluated from the weight gained (0.23 g/g of polymer, see Experimental for details). The FTIR spectra of β -HETP loaded P(NaSS-MBAM) [Fig. 10(a)] and of its poly(MDI-TEG) coated product [Fig. 10(b)] reveal the presence of the corresponding absorption bands of the carbamate group ($-\text{NHCOO}-$) at 1705 and 1658 cm^{-1} , and of the ethylene glycol group ($-\text{CH}_2-\text{O}-\text{CH}_2-$) at 1050 and 1112 cm^{-1} .

A preliminary study of drug delivery in a static water system was conducted by using β -HETP loaded P(NaSS-MBAM) and its poly(MDI-TEG) coated particles (Fig. 11). The released fraction in Figure 11 indicates the weight ratio of β -HETP in the aqueous solution to the initial amount in the particles. As expected, the figure shows that the presence of the poly(MDI-TEG) coating layer reduces the delivery rate.

CONCLUSION

Two coating methods, based on different kinds of interfacial polymerization, are proposed to cover hydrogel latexes with a polymer layer.

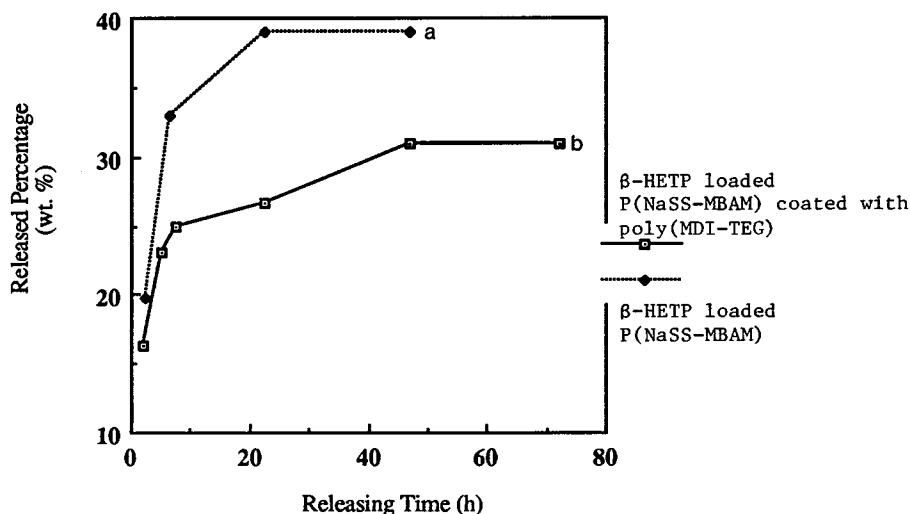


Figure 11 Time dependence of the matrix delivery of β -HETP in water from (a) β -HETP loaded P(NaSS-MBAM); (b) β -HETP loaded P(NaSS-MBAM) coated with poly(MDI-TEG).

1. A proton acid catalyst is trapped inside hydrogel latexes, and the suspension of the catalyst-containing latexes in an organic medium containing an alkyoxyl metal compound generates an interfacial sol-gel process. As a result, a metal oxide will cover the hydrogel latex particles.
2. TEG is deposited on the surface of hydrogel particles, and subsequently, the stirring of PEG deposited hydrogel particles in a low polar organic medium containing a diisocyanate and a suitable catalyst casts a PU layer on the surface of the hydrogel particles.

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