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Preparation of 2-Methacryloyloxyethyl Phosphorylcholine Copolymers with Alkyl Methacrylates and Their Blood Compatibility

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ABSTRACT: Copolymers having the phospholipid polar group, 2-methacryloyloxyethyl phosphorylcholine (MPC) and alkyl methacrylates (*n*-butyl, *tert*-butyl, *n*-hexyl, *n*-dodecyl, and *n*-stearyl groups) were synthesized. The characteristics of these copolymers and blood cell adhesion on the copolymers were investigated. Solubility in various solvents, glass transition temperature, and swelling degree in water depended not only on their MPC composition but also on alkyl groups of the comonomer. Copolymer surfaces were equilibrated in water within a day except for poly(MPC-*co*-*n*-stearyl methacrylate), which was confirmed by dynamic contact angle measurements. Deposition of fibrin and adhesion of blood cells on the MPC copolymers after contact with whole blood were strongly influenced by MPC composition and chemical structure of the copolymer, but there was no relationship between surface free energy and blood compatibility. The blood compatibility of these MPC copolymers also changed based on the substrate membrane which was coated with the MPC copolymers. That is, when poly(*n*-butyl methacrylate) was used as the substrate membrane, poly(MPC-*co*-*n*-dodecyl methacrylate) did not show good blood compatibility, whereas the blood compatibility of the copolymer was improved on a polyethylene substrate. The affinity of MPC copolymers to the substrate is thought to be one of the dominant factors that determine the blood compatibility of the copolymers.

KEY WORDS 2-Methacryloyloxyethyl Phosphorylcholine / Alkyl Methacrylate / Copolymerization / Water Content / Coating / Peel Adhesion Test / Dynamic Contact Angle / Blood Compatibility / Cell Adhesion / Phospholipid /

For development of nonthrombogenic and blood compatible polymers, we proposed a new concept, an artificial surface which is very similar to a biomembrane surface that has excellent nonthrombogenicity.[1] Therefore, a methacrylate having a phosphorylcholine moiety, 2-methacryloyloxyethyl phosphorylcholine (MPC), was synthesized and copolymerized with various methacrylates and styrene.[2–4] In these copolymers, the blood compatibility of poly[MPC-*co*-*n*-butyl methacrylate(BMA)] was investigated in detail. Thus, poly(MPC-*co*-BMA) effectively suppressed the adhesion and activation of blood cells when it contacted both platelet-rich plasma[5,6] and whole blood[7]. The amount of plasma proteins adsorbed on poly(MPC-*co*-BMA) was much lower than that on glass, poly(BMA) or poly[2-hydroxyethyl methacrylate (HEMA)] which is a typical hydrogel.[8,9]

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We assumed that if the types of hydrophobic monomers which were copolymerized with MPC were changed, the character of the MPC copolymers would be drastically different. For example, MPC copolymers can be used as coating materials of commercial artificial organs. When the solubility of MPC copolymers for solvents is changed with different alkyl methacrylates, the application of MPC copolymers can be spread for many materials that consist of various substrates. In this article, the basic properties and blood compatibility of MPC copolymers with alkyl methacrylate are described.

EXPERIMENTAL

Materials

MPC was synthesized by a previously reported method.[2] The structure is shown in Figure 1. BMA, *tert*-butyl methacrylate (tBMA), *n*-hexyl methacrylate (HMA), *n*-dodecyl methacrylate (DMA), and HEMA were purified by vacuum distillation in an argon atmosphere and fractions of bp 68.5°C/30 mmHg, 67°C/70 mmHg, 51—52°C/2 mmHg, 123—124°C/1 mmHg, and 63°C/3 mmHg were used, respectively. *n*-Stearyl methacrylate (SMA) and α,α′-azobisisobutyronitrile (AIBN) were used without further purification.

Synthesis and Characterization of Poly(MPC-co-alkyl methacrylate)

The desired amounts of MPC, alkyl methacrylate, and AIBN were dissolved in a solvent and the solution was poured into polymerization tubes. The concentration of monomers and AIBN were 1.0 mol l^{-1} and 1.0×10^{-3} mol l^{-1}, respectively. After oxygen in the tubes was eliminated by bubbling argon through the solution, the tube was sealed. The tube was then shaken at 60°C for 15 h. The contents were cooled to stop the reaction and poured into a large amount of poor solvent to precipitate a polymer. The precipitated polymer was collected and dried *in vacuo*.

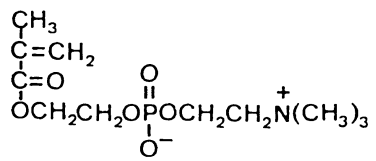

Figure 1. Structure of 2-methacryloyloxyethyl phosphorylcholine(MPC).

Characterization of MPC Copolymers

The structures of the copolymers were characterized by IR and ^{1}H NMR spectra. The mole fraction of the MPC moiety in the copolymers was determined by phosphorus analysis[10]. The molecular weight of the copolymers was estimated using size-exclusion chromatography with a polystyrene standard (column, Asahipak GS-510; eluent, chloroform–ethanol = 6 : 4). Differential scanning calorimetry (DSC) was performed using a SEIKO DSC-100 at a heating rate of 10°C min^{-1}. The glass transition temperature (T_g) was obtained at the inflection point of the DSC curve. Solubility tests were conducted with polymer concentrations of approximately 1% (w/v) at room temperature.

Measurement of the Equilibrium Water Content of the Polymer Membrane

The membranes of the MPC copolymers were prepared by the solvent evaporation method as follows: five milliliters of solution containing 0.5 g of copolymer was cast on a polyethylene plate at room temperature for 1 day, and then for removal of all traces of solvent, the membrane was dried *in vacuo*.

The polymer membrane was immersed in distilled water and swollen in a thermostated vessel. The swollen membrane was taken off and excess solution was removed by lightly tamping it between filter papers. The membrane was then weighed. The equilibrium water content (H) was calculated using the following equation:

$$H = \frac{\text{(weight of water in the membrane)}}{\text{(weight of membrane swollen)}}$$

Dynamic Contact Angle Measurements

The contact angle hysteresis of the copolymers was measured using the dynamic Wilhelmy plate technique (Orientec Co., Ltd., DCA-20). The copolymer was coated on a poly(ethylene telephthalate)(PET) membrane ($25 \times 50 \times 0.35$ mm) which had been cleaned by sonication in acetone for 5 min. The polymer coating was achieved by a solvent evaporation technique using a 0.5 wt% polymer solution. The polymer-coated membrane was dried *in vacuo* for a day at room temperature. The contact angle hysteresis curve was expressed by plotting the interfacial tension versus the immersion depth. The crosshead speed was 10 mm min^{-1}. The dynamic contact angle was calculated according to a procedure reported by Andrade *et al.*[11] The membranes immersed in water for a day were also measured.

Peel Adhesion Test

The peel adhesion test was performed according to the ASTM standard method.[12] The cast membranes of MPC copolymers having a thickness between 100 μm and 121 μm were cut 2 mm apart and a total of six cuts were made. All cuts were under 2 cm long. Pressure-sensitive poly(vinyl chloride) (PVC) adhesive tape for electrical insulation (Showa Denko Co. Ltd.) with a width of 1.9 mm was for contact with the membrane. After rubbing the tape firmly with a pencil eraser, the tape was removed by seizing the free end and rapidly pulling it off at as close to an angle of 180° as possible. The grid area for removal of the coating from the substrate was inspected. The tests were performed at least nine times for each sample.

Evaluation of Blood Compatibility

Polymer membranes of poly(BMA), poly(HMA), and polyethylene were coated with the MPC copolymers by the solvent evaporation technique using a 0.5 wt% polymer solution. X-ray photoelectron spectroscopic (XPS) analysis with a Shimadzu ESCA-750 was carried out to determine the MPC composition of the polymer-coated membrane's surface. The MPC composition was calculated from the ratio of phosphorus atoms versus carbon atoms. Disks (15 mm) of the MPC copolymers punched from the polymer-coated membrane were placed into the wells of Falcon 24-well tissue culture plates and secured by placing a silicone rubber ring on top of the material. A phosphate buffered saline (PBS, pH 7.4) was allowed to stand in the wells for a day to equilibrate the surface. Whole blood prepared from Japanese white rabbits weighing about 3.0 kg was prepared as follows: the carotid artery was cannulated using PVC tubing and 90 ml of fresh blood per rabbit was collected in a disposable syringe containing 10 ml of a 3.8 wt% aqueous sodium citrate solution. Re-activated blood induced by calcium ions was prepared by the addition of 178 μl of 1 mol l^{-1} $CaCl_2$ aqueous solution into the 10 ml of citrated blood. The final concentration of Ca^{2+} in the re-activated blood was 2.5 mmol l^{-1}

The blood (0.7 ml) was poured on the test materials and incubated for given times at 30°C. After the blood was removed, the test materials were twice rinsed with PBS and then placed in a saline solution containing 2.0 wt% glutaraldehyde to fix the biological components adhered on the materials. The materials were sufficiently rinsed with distilled water, freeze-dried with liquid nitrogen, and coated with gold. The surface of the materials was observed using a scanning electron microscope (SEM, JEOL JSM-5400).

RESULTS AND DISCUSSION

Chracteristics of MPC Copolymers with Alkyl Methacrylate

MPC is a water-soluble monomer and its homopolymer is also water soluble. The results

Table I. Synthesis and characterization of MPC copolymers

Abb.	Alkyl methacrylate	MPC mole fraction in feed	MPC mole fraction in copolymer	Solvent	Conv. %	M_w (10^4)	M_w/M_n	T_g °C	H^c	MPC mole fraction coated on poly(BMA)
M13-B	BMA	0.20	0.13	EtOH/THF=8/2	78	—	—	31	—	0.21
M26-B	BMA	0.40	0.26	EtOH	70	—	—	—	—	0.34
M40-B	BMA	0.60	0.40	EtOH	76	1.63	1.42	63	—	—
M58-B	BMA	0.80	0.58	EtOH	74	1.79	1.47	—	—	—
M18-tB	tBMA	0.20	0.18	EtOH/THF=8/2	81	3.63	1.69	—	0.388	0.21
M31-tB	tBMA	0.40	0.31	EtOH	56	—	—	—	0.719	0.32
M48-tB	tBMA	0.60	0.48	EtOH	68	—	—	—	—	—
M66-tB	tBMA	0.80	0.66	EtOH	80	—	—	—	—	—
M11-H	HMA	0.20	0.11	EtOH/THF=8/2	39	6.51	1.04	5	0.650	0.22
M24-H	HMA	0.40	0.24	EtOH	71	—	—	—	—	0.34
M31-H	HMA	0.60	0.31	EtOH	23	—	—	—	—	—
M35-H	HMA	0.80	0.35	EtOH	78	—	—	52	—	—
M14-D	DMA	0.20	0.14	EtOH/THF=5/5	66	—	—	−30	—	—
M20-D	DMA	0.40	0.20	EtOH/THF=5/5	31	7.71	1.05	−16	—	0.35
M38-D[a]	DMA	0.60	0.38	EtOH/THF=9/1	44	—	—	−11	—	0.47
M05-S	SMA	0.20	0.05	EtOH/THF=3/7	83	—	—	—	0.172	—
M28-S	SMA	0.40	0.28	EtOH/THF=6/4	62	22.9	1.30	39[b]	0.373	—
M49-S	SMA	0.60	0.49	EtOH/THF=9/1	46	—	—	39[b]	0.576	—
M69-S	SMA	0.80	0.69	EtOH/THF=9/1	60	—	—	—	—	—

[a] Polymerized for 6 h.
[b] Melting point.
[c] Equilibrium water content.

of the copolymerization of MPC and alkyl methacrylate are summarized in Table I. The solubility of these MPC copolymers is listed in Table II. In this table, "Swelling" means that a membrane with large volume change with swelling, while "Insoluble" means that a membrane without large volume changes.

The radical copolymerization of MPC with alkyl methacrylate proceeded satisfactorily in every case. MPC composition in the copolymers increased with feed. The molecular weight of the obtained poly(MPC-*co*-alkyl methacrylate) was at least 1.6×10^4. T_g of the copolymers increased with mole fraction of MPC. However, it decreased as the alkyl chain length of alkyl methacrylate increased. The membranes obtained by casting were soft in M13-B, M26-B, M18-H, M31-H, and poly(MPC-*co*-DMA)s. This was due to the low T_g of these MPC copolymers. The T_g of poly(MPC-*co*-tBMA) could not be successfully measured, but it is suggested that the T_g is higher than poly(MPC-*co*-BMA) with the same MPC composition from comparison of the T_g of poly(tBMA) and poly(BMA). This was also confirmed from the difference in membrane processability between poly(MPC-*co*-tBMA)s and poly(MPC-*co*-BMA)s. When the solvent was evaporated, the poly(MPC-*co*-tBMA) membrane cast on the polyethylene dish condensed and the obtained membrane was very brittle at room temperature. The poly(MPC-*co*-SMA) had a melting point because SMA is crystalline at room temperature. The crystalline structure and melting point of poly(MPC-*co*-SMA) were also determined by Nakaya *et al*[13].

Since the MPC moiety is hydrophilic, MPC copolymers took the hydrogel structure in water. For example, poly(MPC-*co*-BMA) which mole fraction was below 0.4 became hydrogels, and these became water-soluble

Table II. Solubility of MPC copolymers

	H_2O	EtOH	$CHCl_3$	THF	Et_2O	HFIP[a]
SP[b] (10^{-3} $J^{1/2}$ $m^{-3/2}$)	47.9	26.0	19.0	18.6	15.1	—
M13-B	−	+	+	±	±	
M26-B	−	+	±	−	−	
M40-B	+	+	−	−	−	
M58-B	+	+	−	−	−	
M18-tB	−	+	+	±	±	−
M48-tB	+	+	−	−	−	
M66-tB	+	+	−	−	−	
M11-H	±	+	+	+	±	
M24-H	±	+	±	−	±	+
M35-H	+	+	−	−	−	
M14-D	−	−	±	±	−	±
M20-D	±	+	+	−	−	±
M38-D	−	+	±	−	−	±
M05-S	−	−	±	±	−	
M28-S	−	−	+	±	−	
M49-S	−	±	±	−	−	
M69-S	±	+	±	−	−	

[a] Hexafluoro-*iso*-propanol.
[b] Solubility parameter.
+, soluble; −, insoluble; ±, swelling.

when the MPC composition increased to 0.4. We have already reported that the poly(MPC-*co*-BMA) membranes in the hydrogel state show unique properties; that is, hydration increases with temperature.[2,14,15] This is the opposite tendency for general hydrogel membranes with amphiphilic structures. The solubility in organic solvents depends on both the MPC composition and chemical structure of alkyl methacrylates.

A M20-D membrane adhered to glass even in water. It was hard to release the M14-D membrane from a polyethylene dish. Glass has a very hydrophilic surface, whereas polyethylene is hydrophobic. These results are interesting since it appears that the composition of the MPC copolymers influences the adhesiveness of the copolymers to the substrate. The peel adhesion test quantitatively showed this phenomena. The average area of residue on the polyethylene was at least 32% in the M14-D case, but M13-B, M11-H, and M18-tB would not adhere to the polyethylene surface. Moreover,as the composition of alkyl methacrylate increased, the adhesion on polyethylene became harder even for the poly(MPC-*co*-DMA) case. This result means that the DMA moiety has affinity for the polyethylene.

The Solubility parameter of polyethylene is in the range of $(16—18) \times 10^{-3}$ $J^{1/2}$ $m^{-3/2}$, that of poly(octyl methacrylate) is 17×10^{-3} $J^{1/2}$ $m^{-3/2}$, and that of poly(SMA) is 16×10^{-3} $J^{1/2}$ $m^{-3/2}$.[16] The solubility parameter value decreased with increasing alkyl chain length in alkyl methacrylate. The value for poly(DMA) was thought to be almost the same as that for polyethylene. For this reason, there was good affinity between polyethylene and poly(MPC-*co*-DMA) whose DMA composition was high. In this study, we used polymethacrylates and polyethylene membranes as substrates for making test materials for the blood compatibility evaluation. When the polymers are used as a coating for the medical devices to improve the surface properties of the device, the solubility of the polymers and affinity of the polymers *versus* the device surface are important factors for creating a smooth coating layer and to avoid elution or detachment of the coated polymer. It is very important that the solubility and affinity of MPC copolymers can be easily regulated by changing the comonomer species.

Surface Properties of the MPC Copolymers

To evaluate the performance of biomedical polymers, contact angle measurement has been applied. Especially, the dynamic contact angle of the polymer surface has been measured in recent years to obtain information on surface molecular mobility, surface roughness and surface heterogeneity.[17] The surface free energy is considered to be one of the dominant factors determining the interaction between blood components and the polymer surface.[18] Andrade *et al.* reported a correlation between

the surface concentration of adsorbed human low density lipoprotein (LDL) and the receding contact angle of the polymer surface. The hydrophobicity of the polymer appeared to be correlated with the increased adsorption of LDL.[19] Takahara et al. made surface analysis of segmented poly(urethaneurea)s included the dynamic contact angle and XPS, and blood compatibility.[20] The hydrophilic side chains were located at the aqueous interface and the existence of ions in water influenced the dynamic contact angle loops.[21] They also measured the dynamic contact angle of the surface of poly(urethaneurea)s after exposure to bovine serum albumin (BSA).

Figure 2 shows the dynamic contact angle loops of a PET membrane at 20°C. The second cycle traced the first cycle completely. After the PET membrane was immersed in water for a day, the contact angle did not change before immersion. Figure 3A shows the dynamic contact angle loops of the M26-B membrane. The loops did not become stable during measurement. The advancing contact angle-(θ_{adv}) of the M26-B membrane kept larger from second cycle and the receding contact angle (θ_{rec}) kept smaller. This shows that the swelling of the M26-B and the following as the reorientation of molecules did not occur immediately. The curves after a one-day immersion in water became stable as shown in Figure 3B. The contact angle hysteresis of M26-B was large ($\Delta\theta = 92°$). The curves of other copolymers except poly(MPC-*co*-SMA) also became stable after immersion for a day. Table III shows the advancing and receding contact angles and hysteresis of each copolymer after a one-day immersion. All hystereses were large (61—100°) compared with the PET. The receding contact angles of the surfaces coated with these MPC copolymers were almost the same value. The advancing contact angles of these copolymers were different in different mole fractions of copolymers even if the same alkyl methacrylate was used. The value of the advancing contact angle had no simple relation to structures on the characteristics of the copolymers. The hydrophilic components of hydrogels and the microphase separated

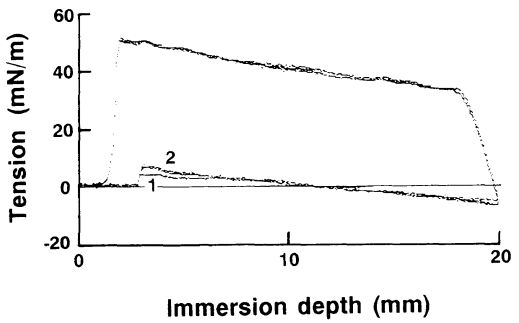

Figure 2. Dynamic contact angle measurement of PET film.

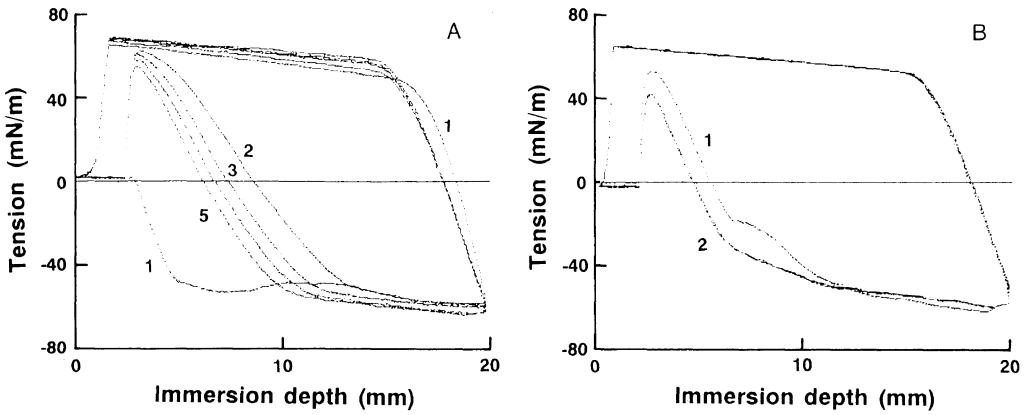

Figure 3. Dynamic contact angle measurement of M26-B-coated membrane.

Table III. Dynamic contact angles and hystereses of MPC copolymers-coated membrane

	θ_{adv}	θ_{rec}	$\Delta\theta$
	°	°	°
Control (PET)	83	45	38
M13-B	109	28	81
M26-B	123	31	92
M18-tB	90	24	66
M31-tB	118	28	90
M11-H	114	25	89
M24-H	127	27	100
M20-D	123	27	96
M38-D	110	23	87
M28-S	82	21	61
M49-S	88	24	64
M69-S	94	24	70

surface generally influenced the receding contact angle.[22] MPC copolymers coated on PETs largely swelled and the phosphorylcholine moiety of MPC was oriented to the water side. This phosphorylcholine moiety dominates the value of receding contact angle.

Holly and Refojo observed that the chains of poly(HEMA) hydrogel could undergo significant rotation according to the environment to minimize the interfacial energy.[23] This mobility of molecular was thought as the reason for a large hysteresis. The same phenominon was observed in the case of MPC copolymers.

Blood Compatibility

Figure 4 shows SEM pictures of poly(BMA) membranes coated with MPC copolymers after contact with whole blood. Fibrin deposition and cell adhesion were observed on poly(BMA). On poly(HEMA), cell adhesion was also found. In the case of the MPC copolymers, fibrin deposition and cell adhesion were reduced with increase in MPC composition except for poly(MPC-*co*-DMA). In particular, there was no fibrin deposition on the M26-B surface. In a previous article, we investigated platelet adhesion on poly(MPC-*co*-BMA)s using a microsphere-column method and observed that there was no platelet adhesion and activation on the copolymer with a 0.32 MPC mole fraction.[5] The results found in this study were confirmed by results from the microsphere-column method.

Attention was then paid to the effects of alkyl chain length of the alkyl methacrylate on blood compatibility by comparison of M26-B, M31-tB, M24-H, and M20-D, whose surfaces had MPC compositions of the value of 0.32—0.35. Blood compatibility became poor when the length of *n*-alkyl group increased. Though M31-tB has the same carbon numbers as M26-B, much fibrin deposition and cell adhesion were observed.

Both the advancing and receding contact angles on M26-B, M24-H, and M20-D were almost the same, but blood cell adhesion and activation differed significantly. Thus, surface wettability is not a suitable parameter to estimate the blood compatibility of MPC copolymers, even some investigators have discussed that blood compatibility and protein adsorption are related to the wettability of a material surface.[24,25] It is clearly shown that blood compatibility depends on the very small differences in the chemical structures of the MPC copolymers. We already reported that blood cells did not adhere and activate on poly(MPC-*co*-BMA). However, a lot of cells adhered and aggregated on other hydrophilic-hydrophobic random copolymers such as poly(acrylamide-*co*-BMA), poly(2-acrylamide-2-methylpropane sulfonic acid-*co*-BMA), and poly(*N*-vinylpyrrolidone-*co*-BMA) even though they have almost the same hydration.[6]

One more important point to consider is the effects of substrates, because the properties of the substrate strongly affects the orientation and/or distribution of a MPC unit. Therefore, test materials for the blood compatibility experiments were prepared by coating them on poly(HMA) and polyethylene membranes.

On poly(HMA) membranes coated with MPC copolymers, lower blood cell adhesion was observed not only on poly(MPC-*co*-

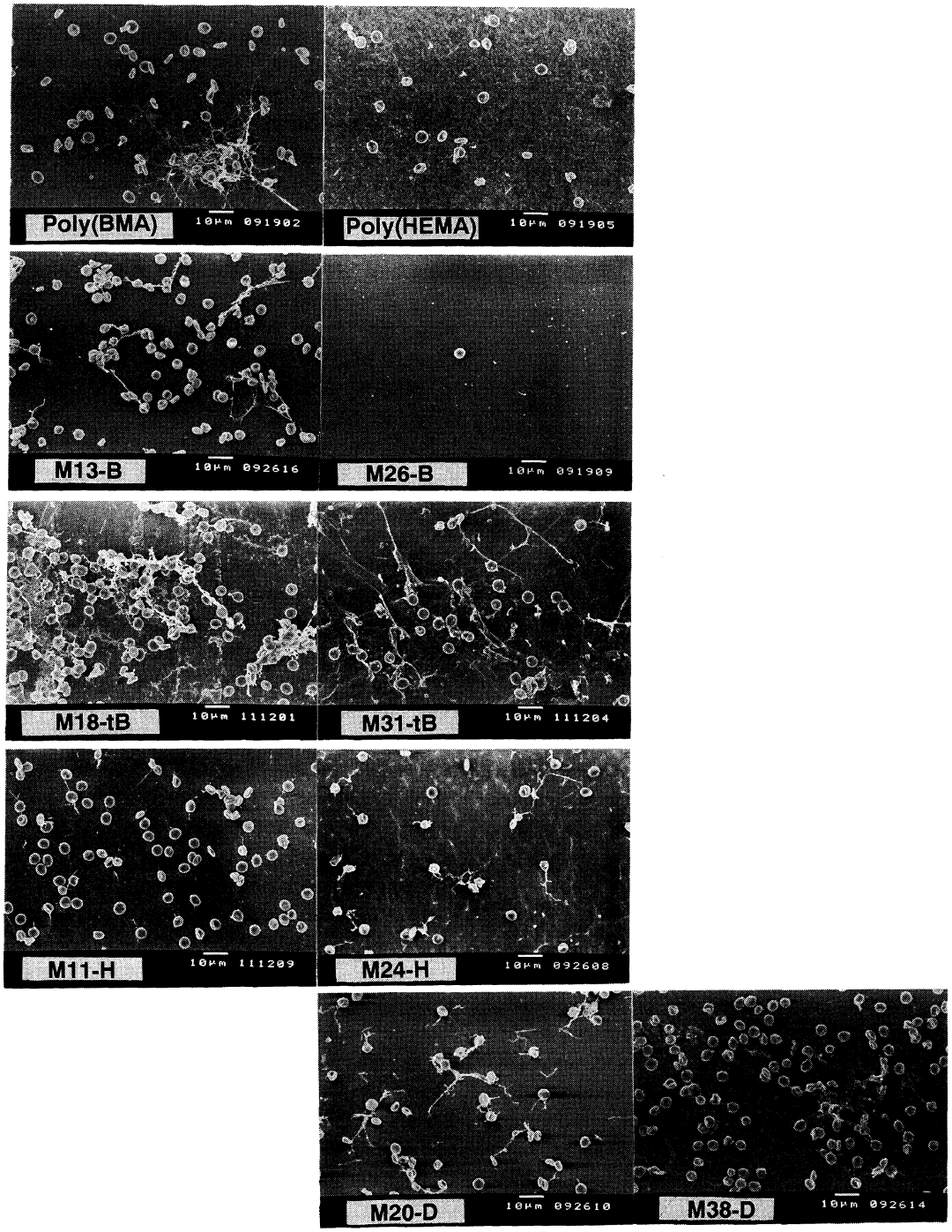

Figure 4. SEM view of the surface of poly(BMA) coated with MPC copolymers after contact with rabbit re-activated whole blood for 60 min.

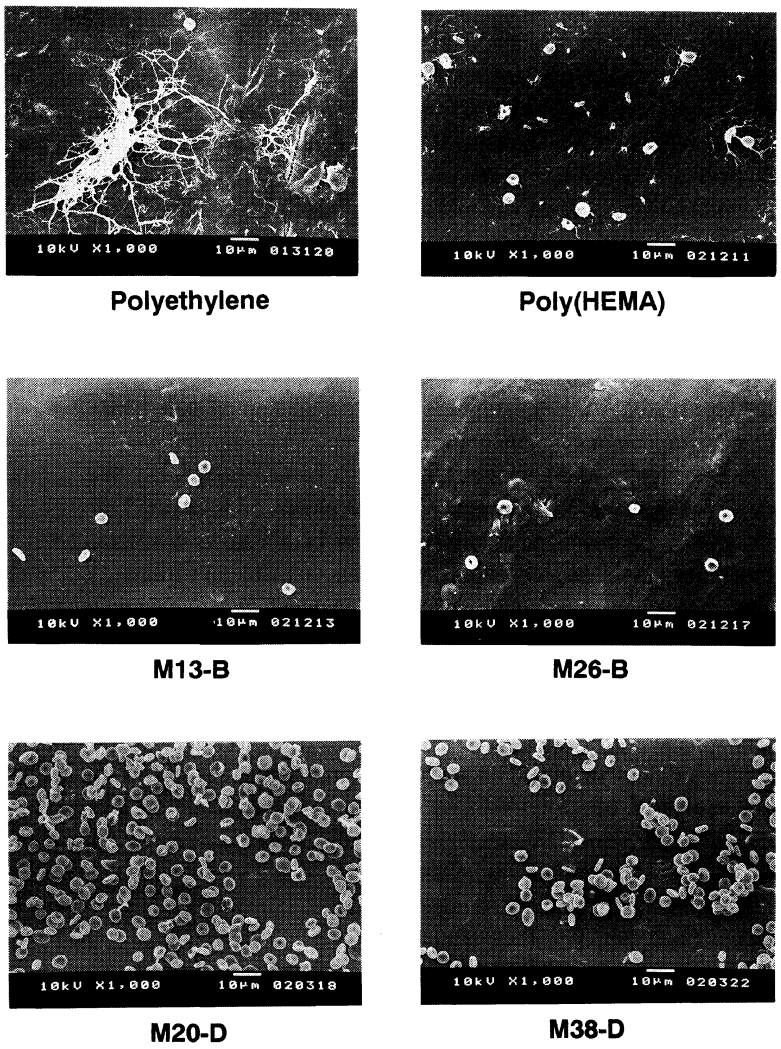

Figure 5. SEM view of the surface of polyethylene coated with MPC copolymers after contact with rabbit re-activated whole blood for 60 min.

BMA)s but also on poly(MPC-*co*-HMA)s.

Figure 5 shows SEM pictures of polyethylene membranes coated with MPC copolymers after contact with blood. On a non-treated polyethylene surface, fibrin deposition and cell adhesion were found. When the surface was coated with poly(MPC-*co*-BMA), blood compatibility was drastically improved. Recently, Xi *et al.* reported platelet adhesion on polyethylene tubing coated with poly(MPC-*co*- BMA) and biomedical segmented polyurethanes.[26] They indicated that the surface of poly(MPC-*co*-BMA)-coated polyethylene showed significantly better platelet adhesion resistance than these polyurethanes. Though blood cell adhesion was found on M38-D-coated polyethylene, there was no fibrin deposition. A cell adhesion experiment was carried out using platelet-rich plasma(PRP). When the surface of polyethylene was in

contact with PRP, about $3.5 \times 10^4/mm^2$ platelets adhered and were activated. On the other hand, M38-D-coated polyethylene suppressed the adhesion of the platelets. Poly(MPC-*co*-DMA) showed good blood compatibility with polyethylene. A peel adhesion test indicated that poly(MPC-*co*-DMA) has affinity to polyethylene whereas poly(MPC-*co*-BMA) does not. Thus, the DMA unit in poly(MPC-*co*-DMA) plays an important role in affinity. It is suggested that since the longer alkyl chains of DMA directly contact the polyethylene surface, MPC units are concentrated on the water side. This provides an improvement in blood compatibility on a polyethylene surface by coating it with poly(MPC-*co*-DMA).

Regarding the effects of MPC copolymers on blood compatibility, we reported that the phosphorylcholine moiety in copolymers was oriented to the water side using by XPS when the surface coated copolymers were immersed in water.[6] The MPC moieties have strong affinity to phospholipid molecules even in plasma and the arrangement of phospholipids adsorbed on the surface of poly(MPC-*co*-BMA) was indicated by XPS and DSC analyses when the surface was treated with a liposome solution of phospholipid.[27,28] That is, the biomembrane-like surface, which gathers phospholipid molecules, is considered to be built up on the MPC copolymer surface. This is the most dominant factor for blood compatibility appeared on the MPC copolymers. Moreover, the adsorption of plasma proteins was reduced on MPC copolymers as compared to other acrylic polymers including poly(HEMA).[8,9,14] This protein adsorption resistance property is another reason for blood compatibility according to Kim *et al.*[29] and Okano *et al.*[30]

Very recently, we found that the adsorption of proteins from human plasma decreased with increase in the MPC composition in every MPC copolymer, which completely corresponds to increase of phospholipid adsorption on these copolymer.[31]

In conclusion, we synthesized the copolymers of MPC and alkyl methacrylate, and characterized their basic properties. The characteristics of MPC copolymers was largely different using different alkyl methacrylate. The solubility of MPC copolymers largely depends on the mole fractions and kinds of alkyl methacrylates. This shows that MPC copolymers are used as coating materials for many kinds of substrates. The blood compatibility of substrate membrane increased by coating adequate MPC copolymers whose solubility parameter of alkyl methacrylate was almost the same as that of substrate.

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