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Preparation of block copolymer of poly(trimethylene carbonate) with oligo (ethylene glycol) and the surface properties of the dip coated film

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ABSTRACT

To persuade the stent coating materials for the better sustainable development, a block copolymer composed of hydrophobicity of poly(trimethylene carbonate) (PTMC) and hydrophilicity of PTMC bearing ethylene glycol chains was synthesized as a potential candidate. The result of thermal stability of the polymer was analyzed which reached up to 206 °C (T_{10}) and it is considered that sufficient for sterilization during the treatment. Moreover, the dip coated films of polymer were coated on polyethylene (PE) and stainless steel (SS) substrates in order to stimulate the stability upon the physiological environment. In addition, the preliminary *in vitro* test of the films were evaluated by protein adsorption and blood platelet adhesion tests. Hence, this study tends to convince that the synthetic block copolymer based on PTMC derivatives were approached for stent coating materials.

1. Introduction

Stent coating materials are mainly enhanced to cover the stainless steel (SS) stents [1,2] and polyethylene (PE) balloons [3–5], which are attractive and utilized in clinical treatment. Due to blood vessels therapy, the novel materials which compose biocompatibility with low toxicity and biodegradable properties are typically developed. Poly (trimethylene carbonate) derivative or (PTMC) derivative is one of the potential candidate polymer because their outstanding performance with the low crystallinity.

Biodegradable PTMC derivatives are coming up with cutting-edge and variety of purpose at present· [6–8] Due to their unique degradation behavior [9,10], there was no acidic compound generate of the polymer against stimuli circumstance. It is known that PTMC is synthesized by ring-opening polymerization (ROP) [11] using various kind of catalysts such as organic [12], inorganic [13] and enzyme [14]. There have already been reported on PTMC derivatives researches with respect to inspect of fundamental attributes, mechanical properties [15], particular polymer characteristics [16–18] and biocompatibilities [19, 20], and developments for biomaterial applications, such as scaffolds [21,22], tissue engineering [23–25], drug delivery systems [26–28] and vascular grafts [29,30]. The PTMC derivatives have been developed by the side group modification upon molecular design as well. However, the aforementioned PTMC derivatives usually possess ester groups at the side chain [7,8] in spite of non-acid generation from the polymer chain. Our group was motivated to design the ester-free structure, because it would be better to totally exclude the acid generation during degradation process. Therefore, secured PTMC derivatives with ester-free side chain modification was developed to approach the low-toxicity biomaterial.

The synthetic PTMC derivatives bearing hydrophilic side chain have previously been reported [31–34]. For example, the thermosensitive behavior, lower critical solution temperature (LCST), was introduced to broaden the area of biomaterial applications [35]. Importantly, trimethylene carbonate (TMC) derivatives bearing oligo(ethylene glycol) (OEG) units, 5-[2-{2-(2-methoxyethoxy)ethoxy}ethoxymethyl]-5--methyl- [1,3]-dioxa-2-one (TMCM-MOE3OM) and 5-ethyl-5-(2,5,8,11, 14-pentaoxapentadecyl)-1,3-dioxan-2-one (TMCE-MOE4OM), were designed to control the balance of the hydrophilic OEG side chain and the hydrophobic polymer main chain. Then, thermosensitive polymers which were synthesized using TMCM-MOE3OM and TMCE-MOE4OM with 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) as catalysts. The lower critical solution temperature (LCST) or phrase transition change temperature were showed at around 33 °C for poly(TMCM-MOE3OM) and

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37 °C for poly(TMCE-MOE4OM) [31]. Thus, the LCST control around body temperature could achieved by a molecular design. Both PTMCM-MOE3OM and PTMCE-MOE4OM were in liquid-like state and water soluble polymers. Although biodegradable block copolymers [36–39] and random copolymers [39–41] of PTMC with poly (lactic acid) (PLA) have been investigated for biomaterials, such as scaffolds [42,43] and tissue engineering [44]. By the way, the PLA and PTMC copolymer is rather found the acidic residue generation upon degradation period, which may relate to the ester group along the PLA main chain. Therefore, our motivation still keep toward the preparation materials based on PTMC backbone consisting of hydrophobic and hydrophilic block copolymer.

In this study, a block copolymer PTMCM-MOE3OM-*b*-PTMC were synthesized by ring-opening polymerization of TMC monomer with DBU catalyst and PTMCM-MOE3OM as a macro initiator to engage the development of surface coating materials. To spread the range of application especially blood vessels treatment, the hydrophobic PTMC was introduced to hydrophilic PTMCM-MOE3OM. The structure of the block copolymer, PTMCM-MOE3OM-*b*-PTMC, was basically confirmed by ^{1}H NMR spectroscopy, size exclusion chromatography (SEC) trace, and physical properties by thermogravimetric analysis (TGA) curves and rheometry. Furthermore, the dip coated films on SS and PE substrate were prepared in order to investigate preliminary biocompatibility test. Hence, the manipulation of SS stents or PE balloons were examined by water drop contact angle measurement, protein adsorption and platelet adsorption tests.

2. Experimental section

2.1. Materials

Benzyl alcohol, and 1,8-diazabicyclo[5.4.0]-7-undecene (DBU) were purchased from Tokyo Chemical Industry (TCI), Japan. Dichloromethane (CH_2Cl_2), hexane, tetrahydrofuran (THF), methanol and isopropanol were purchased from AZBIO CORP, Japan. Calcium hydride (CaH_2) was purchased from Nacalai Tesque Inc, Japan. Benzyl alcohol and DBU were distilled before used. Anhydrous THF and CH_2Cl_2 were distilled with CaH_2 before use.

2.2. Polymerization

2.2.1. Synthesis of PTMCM-MOE3OM

The monomer, TMCM-MOE3OM, was synthesized following our previous research [31]. The obtained monomer was polymerized via ring-opening polymerization with organocatalyst [31]. Briefly, 6 g of TMCM-MOE3OM (20.6 mmol) was dissolved in 40 mL of anhydrous CH_2Cl_2 in the three-necked flask with CaH_2 and stirred overnight. Then, a cannula with glass filter was used to filtrate the supernatant, the monomer solution was transferred to the other flask and the solvent CH_2Cl_2 was evaporated under vacuum atmosphere. To start the polymerization under nitrogen atmosphere, anhydrous CH_2Cl_2 was introduced into the monomer solution, then 1.2 mL of benzyl alcohol (0.104 mmol) solution and 6 mL of DBU (2.06 mmol) solution both in CH_2Cl_2 were added as initiator and catalyst at room temperature for 8 h. The reaction was stopped by adding small portion of acetic acid, then the reaction mixture was poured into a large amount of hexane/2-propanol (9/1, v/v). The product was recovered by decantation and centrifugation and dried under vacuum (19% yield).

2.2.2. Synthesis of PTMCM-MOE3OM-b-PTMC

In the three-necked flask, 0.398 g of PTMCM-MOE3OM (0.118 mmol) was dissolved in 5 mL of anhydrous CH_2Cl_2 with CaH_2 and stir overnight. Using a cannula with glass filter to remove CaH_2, the macroinitiator solution was transferred to the other flask and evaporate the solvent CH_2Cl_2. Then, the anhydrous CH_2Cl_2 was introduced under the nitrogen atmosphere as monomer concentration in Table 1. With a flask of the macro-initiator solution, and 17.7 μL of DBU (0.118 mmol) solution, and TMC (11.8 mmol) solution were added to start the polymerization at room temperature for 8 h. The reaction was quenched by adding small portion of acetic acid, then the reaction mixture was poured into a large amount of hexane/2-propanol (9/1, v/v). The solid was obtained and then dissolved again in CH_2Cl_2 solution and poured into a large amount of methanol. The product was recovered by decantation and centrifugation and dried under vacuum (14% yield).

2.3. Apparatus

^{1}H NMR spectra were measured by a JEOL JNM-ECX400 system. The interfereograms were co-added 64 times and Fourier-transformed at a resolution of 4 cm^{-1}. The Fourier transform infrared spectrometry (FT-IR) spectra were measured using an IRAffinity-1S spectrometer (Shimadzu, Japan). The number average molar masses and their distribution were measured by Size Exclusion Chromatography (SEC). ChromNAV system (JASCO Corporation, Japan) using AS-2055 and RI-2031 was employed with polystyrene (PS) standards at 40 °C (1 mg/mL, 0.6 mL/min). Two commercial columns (TSKgel SuperH3000 and TSKgel GMHXL) were connected in series and tetrahydrofuran was used as an eluent. Thermogravimetric analysis (TGA) was carried out using a Shimadzu TGA-50 from room temperature to 500 °C at a rate of 10 °C/min under nitrogen flow. Time-dependent contact angles were measured by Flow Design CAM-004 contact angle measuring systems and a TOKAI HIT TPX-S applying 2 μL of ion exchange water onto spin-coated films on a glass plate at each temperature.

Protein adsorption tests were carried out for dip coated film on each plate using each peptide, a Micro BCA™ Protein Assay kit (Thermo Fisher Scientific K. K.), and a MTP-310Lab (Corona Electric Co., Ltd.). Each dip coated film was immersed into 900 μL of peptide/PBS solution (4.5 mg/mL) for 4 h at 25 °C. After incubation, films were washed three times with PBS. Then, the films were immersed into 1 mL of SDS/PBS solution (10 mg/mL) for 4 h at 25 °C in order to remove the absorbed protein from samples. The mixture of 400 μL of protein assay bicinchoninate kit and 400 μL of SDS solution containing the protein from the polymer surface was incubated for 2 h at 37 °C. Then, the UV absorbance of the mixture was recorded with a Corona Electric MTP-310Lab. The amount of absorbed protein from the polymer was estimated with UV absorbance by comparing with a calibration curve of the same protein.

Regarding to materials proposal, platelet adhesion test has done preliminarily as the reference procedure.[45] Fresh blood sample was drawn from healthy volunteer. The mixture of 0.1% sodium citrate and blood was centrifuged at 1000 rpm for 7 min to obtain heterogeneous supernatant, platelet-rich plasma (PRP) and platelet poor plasma (PPP). PRP layer was diluted 3-fold with PBS and then platelet concentration (3.0 × 105 cells μL-1) in diluted PRP was determined using fluorescence microscope. The polymer coated substrate (1 cm × 1 cm × 1 mm) were placed at the center of glass petri dish and washed by EtOH and deionized water 3 times, then soaked in PBS for 24 h at 37 °C. The PRP solution was added onto sample and incubated at 37 °C 60 min substrate was washed by PBS solution 3 times and then 2 mL of 2% glutaraldehyde in PBS at 4 °C 2 h. The samples were finally cleansed with 2 mL PBS (3 times) and water, and dried under vacuum overnight. Number of adhered platelets on gel surface was counted and made average by SEM image. Low Vacuum Scanning Electron Microscope (SU6600, Hitachi) was used in condition, accelerating voltage: 1 kV magnification: 1,000x without metal coating of SE signal. Five different areas of sample were captured and counted as average value with standard deviation.

3. Results and discussion

Firstly, TMCM-MOE3OM was synthesized following previously reported methods [33] (Scheme 1, total yield 19%) and it was then polymerized via ROP using DBU as a catalyst (Scheme 2 and Table 1, entry 1). Generally, the molecular weight and the yield of

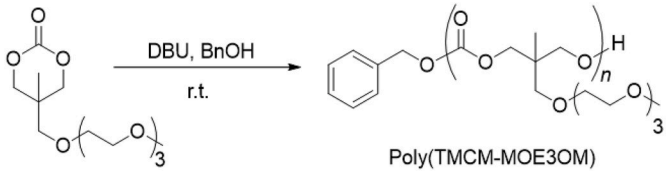
Table 1
Analysis data of PTMCM-MOE3OM and PTMCM-MOE3OM-*b*-PTMC.

Entry	Monomer	Initiator	Concentration (mol/l)	M/I	Yield (%)	*Mn* ($\times 10^3$ g/mol)[c]	PDI[c]
1	TMCM-MOE3OM	BnOH	3.2	200	19[a]	2.6	1.3
2	TMC	PTMCM-MOE3OM	1.0	100	14[b]	4.1[d]	1.6

Catalyst = DBU. M/C = 10.
[a] Hexane: 2-propanol = 9 : 1 (v: v) insoluble part.
[b] Hexane: 2-propanol = 9 : 1 (v: v) insoluble part and then, methanol soluble part.
[c] Determined by SEC by polystyrene (PS) standard in THF.
[d] TMCM-MOE3OM: TMC = 1 : 17 determined by ^{1}H NMR.

PTMCM-MOE3OM could be controlled by the ratio of initiator, and catalyst in term of degree of polymerization [31,33,34]. In order to apply the PTMC derivatives for stent coating and other biomedical materials, the water solubility is mainly considered. Thus, PTMCM-MOE3OM-*b*-PTMC was synthesized by ring-opening polymerization using TMC as a monomer and PTMCM-MOE3OM as an initiator and DBU as catalyst (Scheme 3). Table 1 showed the analytical data for synthesized polymers, PTMCM-MOE3OM (Table 1, entry 1) and PTMCM-MOE3OM-*b*-PTMC (Table 1, entry 2). PTMCM-MOE3OM-*b*-PTMC was purified by twice precipitations. At first, the mixture of hexane: 2-propanol (9:1v/v) was used and then collected the insoluble part which probably was PTMC and PTMCM-MOE3OM-*b*-PTMC mixture. The second precipitation worked with the solubility in methanol and then isolated the supernatant which was PTMCM-MOE3OM-*b*-PTMC.

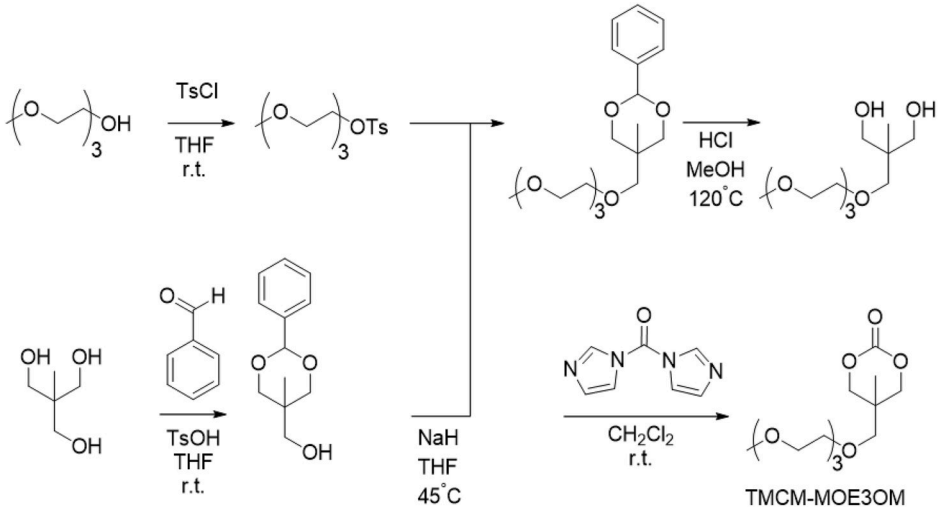
The structure of the block copolymer was asserted by ^{1}H NMR spectroscopy and SEC trace, and interpreted the repeating unit ratio of TMCM-MOE3OM: TMC as 1 : 17, accompanied by an increase in molecular weight after copolymerization (Fig. S1 and S8). The thermal properties of the synthetic polymers were investigated by TGA (Fig. S1). The thermal degradation profile of PTMCM-MOE3OM-*b*-PTMC was about 206 °C at T_{10}, which was defined as the temperature at the 10% weight loss. As the results, PTMCM-MOE3OM-*b*-PTMC provided the lower temperature compared to the homopolymers as PTMCM-MOE3OM (T_{10} 307 °C) and PTMC (T_{10} 228 °C). This probably depends on its chemical structure, degree of crystallinity, and molecular weight during the second polymerization.[47] the chain-end group and side part are considered to make polymer less resistant of thermal stability. However, it was sufficient for sterilization in clinical field by autoclaving (120 °C). For the dynamic moduli, the loss modulus is influenced by the temperature in Fig. S2. The PTMCM-MOE3OM-b-PTMC performs as the materials flowing (G″> G′) at 0 °C and 37 °C. While at low frequency (25 °C), it behaves as an elastic solid or gel-like



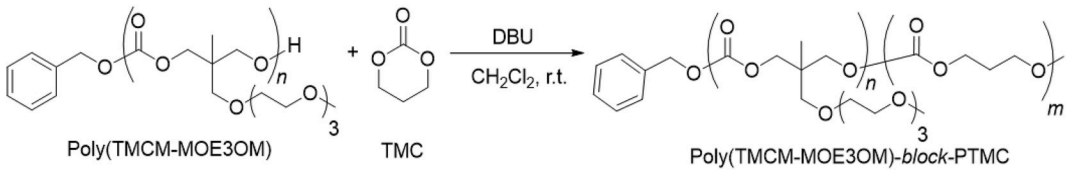
Scheme 2. Synthesis of PTMCM-MOE3OM.

(G′≈ G″) and then becomes fluid materials at high frequency. It was confirmed that the coating materials was sufficient soft and elastic matter.

Next, the basic properties of dip coated films of PTMCM-MOE3OM-*b*-PTMC were investigated to assess their suitability as coating materials. The dip coated films were prepared using PTMCM-MOE3OM-*b*-PTMC on stainless steel (SS, 10 × 10 × 0.1 mm) and polyethylene (PE, 10 × 10 × 1 mm) substrates. SS and PE substrates were treated in EtOH before dip coating preparation. The peeling tests were conducted in PBS and CH_2Cl_2, which were assumed interior liquid of body and negative control (Table 2). As a supplementary, the thickness of the film which was about 0.05 μm, was different depending on the measurement point at least on the SS substrates (Fig. S3). The roughness was probably decreased when dilute the concentration of copolymers and low temperature. The PTMCM-MOE3OM-*b*-PTMC films were then dipped in each solvent for 1 day. The solutions were analyzed by ^{1}H NMR spectroscopy and the films were also analyzed by Fourier Transform Infrared Spectroscopy (FT-IR) (Figs. S4 and S5). The PTMCM-MOE3OM-*b*-PTMC had poor solubility in water thus the film on SS and PE did not well eluent in PBS solution. The confirmation of ^{1}H NMR spectrum in the PBS soluble part (Table 2, entries 1 and 3) was done. In addition, residue of the films on both substrates were also investigated by FT-IR and found the carbonyl peaks of PTMCM-MOE3OM-*b*-PTMC (C═O bond around



Scheme 1. Synthesis of trimethylene carbonate derivatives.



Scheme 3. Synthesis of PTMCM-MOE3OM-*b*-PTMC.

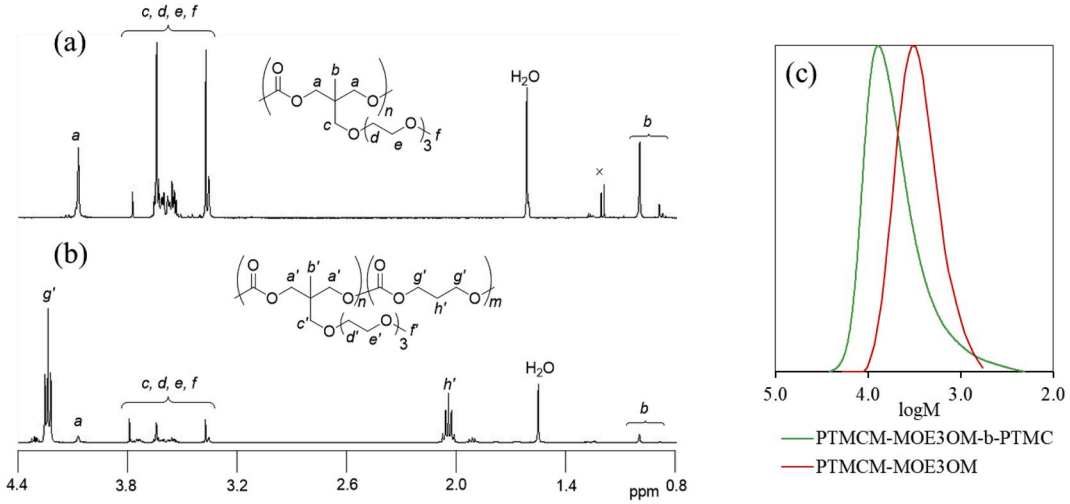


Fig. 1. ^{1}H NMR spectra of PTMCM-MOE3OM (a) and PTMCM-MOE3OM)-*b*-PTMC (b) (400 MHz, r.t., in $CDCl_3$). SEC traces of PTMCM-MOE3OM (c) and PTMCM-MOE3OM-*b*-PTMC (d) (PS standard, THF, 40 °C).

Table 2
Summary of peeling test on each basis.

Entry	Substrate	Solvent	Soluble part ($\times 10^{-2}$ mg)[a]
1	SS	PBS	0.048 ± 0.037
2	SS	CH_2Cl_2	3.1 ± 0.6
3	PE	PBS	0.061 ± 0.059
4	PE	CH_2Cl_2	0.87 ± 0.19

[a] Calculated by the integral value ratio. Determined by ^{1}H NMR.

1740 cm^{-1}).

On the other hand, the film was well eluent in CH_2Cl_2 condition as a good solvent for PTMCM-MOE3OM-*b*-PTMC (Table 2, entries 2 and 4). Thus, the PTMCM-MOE3OM-*b*-PTMC was detected in CH_2Cl_2 by ^{1}H NMR while the carbonyl peaks of PTMCM-MOE3OM-*b*-PTMC were not observed by FT-IR on either SS or PE. These results show that PTMCM-MOE3OM-*b*-PTMC films were appropriate as water soluble materials such as for in-vivo biomedical matter. Furthermore, the amount of rinsed polymers between SS and PE substrates was presented (Table 2, entries 2 and 4) which implied that the polymer compatibility on substrates and media were conducted the potential of film coating properties (see Fig. 1).

A water contact angle test tended to reveal the surface behavior of PTMCM-MOE3OM-*b*-PTMC films. Fig. 2 showed the time dependence contact angle of a water droplet on PTMCM-MOE3OM-*b*-PTMC films on each substrates, SS (Fig. 2A) and PE (Fig. 2B), by which the difference of contact angle values of 72° on bare SS (Fig. 2c and d) and 105° on bare PE (Fig. 2g and h) was observed in condition of no polymer coating. With the difference could be explained by hydrophobicity response.

However, the angle of PTMCM-MOE3OM-*b*-PTMC were shown different degree on substrates, 72° at 0 s on SS (Fig. 2a and b) and 105° at 0 s on PE (Fig. 2e and f) at 25 °C and 45 °C, respectively. It appeared that conformations of PTMCM-MOE3OM-*b*-PTMC on each substrates were probably influenced by substrates surface. Then, the hydrophobic PTMC segments accumulated at the surface and also the hydrophilic PTMCM-MOE3OM segments were moved to the air-polymer interface during the preparation by the dip-coating method.

In addition, the contact angle of PTMCM-MOE3OM-*b*-PTMC film on

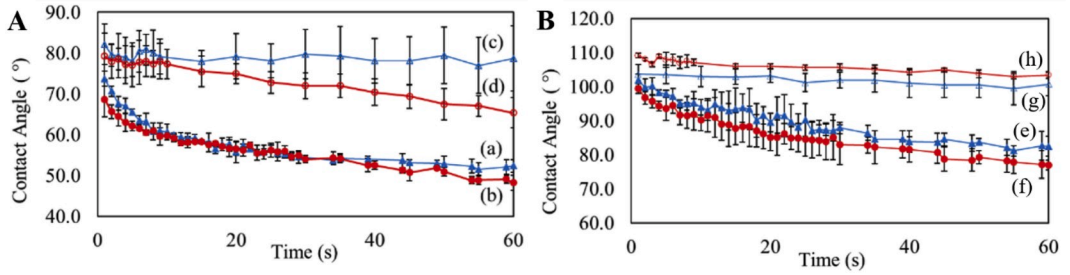


Fig. 2. Time dependence contact angle of water droplet on SS substrate (A) with the dip coated film of PTMCM-MOE3OM-*b*-PTMC at 25 °C (a) and 45 °C (b), and bare SS substrate at 25 °C (c) and 45 °C (d). On PE substrate (B) with the dip coated film of PTMCM-MOE3OM-*b*-PTMC at 25 °C (e) and 45 °C (f), and bare PE substrate at 25 °C (g) and 45 °C (h). (n = 3, CH_3CN, 10 mg/mL).

both substrates slightly become hydrophilic surface by changing from 72° to 52° at 25 °C on SS (Fig. 2a) and 105° to 82.5° at 25C° on PE (Fig. 2e). The above appearance has been already reported in term of interfacial interaction [37]. Initially, the conformation of polymers at the interface were comparatively random on the substrate, and then a water droplet was dropped on the interface. The hydrophilic OEG as side chains at the PTMCM-MOE3OM unit, tended to be free around the interfacial surface of the water droplet. However, their varied values of 20° (Fig. 2a and e, 0s vs 60s), were small compared with previously reported values of about 40°.[37] It was surmised that the ratio of soft segment units (TMCM-MOE3OM) on block copolymer is lower than the previous study [37], which was TMCM-MOE1OM: lactic acid = 1 : 4. The segregated behaviors of the soft segment were prevented by the hydrophobic main chains of TMC units. Regarding to the LCST of PTMCM-MOE3OM homopolymer at around 33 °C [31], therefore the temperature dependence and contact angles of water droplets on PTMCM-MOE3OM-*b*-PTMC were investigated at 25 °C and 45 °C. There were no significant change, however, the result was also referred to the small component of thermosensitive TMCM-MOE3OM segments.

Moreover, to achieve the utility of TMCM-MOE3OM-*b*-PTMC films, the protein adsorption tests was studied to convince the protein repelling surface as desired. Fig. 3 showed the protein adsorption behaviors against PTMCM-MOE3OM-*b*-PTMC and PTMC film on SS or PE substrates. Three kinds of protein such as albumin, globulin and fibrinogen, which are generally composed matter in human blood. The protein adsorption values of PTMCM-MOE3OM-*b*-PTMC tended to be lower than PTMC film and bare substrate. Protein adsorption of films on SS substrate were totally fulfilled in range 0.2–0.7 μg/cm^2 (Fig. 3b), while films on PE substrate were less than 0.2 μg/cm^2 except fibrinogen adsorption values (Fig. 3a). It could explain the influence of the hydrophobicity, the PTMCM-MOE3OM-*b*-PTMC surface were shown contact angle values at 82.5° on PE (Fig. 2a and c, Fig. S6) and 50° on SS (Fig. 2b and c, Fig. S7). Furthermore, trivial differences between PTMCM-MOE3OM-*b*-PTMC and PTMC conveyed the potential of ethylene glycol group at side part of PTMCM-MOE3OM-*b*-PTMC sequence. Besides, the roughness of polymer films was also considered and supported by the result of the peeling test on each substrates (Table 2) and the film thickness evaluation (Fig. S3). The results of protein adsorption test were concluded that the protein adsorption values were influenced by the hydrophobicity and the roughness of polymer films. As positive tendency, PTMCM-MOE3OM-*b*-PTMC block copolymer would be appropriate for utilizing as surface coating material especially on SS and PE.

Platelet adhesion tests were conducted using PTMCM-MOE3OM-*b*-PTMCM and PTMC films on substrates and afterward observed by scanning electron microscopy (SEM) which depicted qualitative differences between the SS (Fig. 4) and PE substrates (Fig. 5). As a denominator, the aggregation of polymer were observed on the film surfaces of SS (Fig. 4a, b, 4c and 4d) and PE (Fig. 5a, b, 5c and 5d) substrates. Konertz (2007) was reported that surface irregularities activated the platelet adhesion. The extent platelet accumulation on rougher surface is higher than smooth matter. PE substrate is stimulated as the smooth balloon surface comparing to PTMC or PTMCM-MOE3OM-b-PTMC. Furthermore, hydrophobic surfaces tend to adsorb larger amount of proteins and platelet than hydrophilicity. However, the observations of surface hydrophilic/hydrophobic transiting at θ = 72–112° (SS substrate) greatly enhance platelet adhesion (Sperling 2009). Therefore, the roughness and hydrophobicity presumably had certain effects on the platelet adsorption behavior.

The image of SS substrates were shown the adhere platelets in flatten shape as corresponding to PTMCM-MOE3OM-*b*-PTMCM (Fig. 4e and f), PTMCM (Fig. 4g and h) and bare substrate (Fig. 4i and j). In addition, the platelet number on PTMCM-MOE3OM-*b*-PTMC film was lower than PTMC and bare one (Fig. 6d, e and 6f). This result indicated that PTMCM-MOE3OM-*b*-PTMC could better approach the prevention of blood clots compared with PTMC and without polymer on the SS substrate. On the other hand, the shapes of platelets on PE material were totally maintained (Fig. 5) a discrete appearance in sphere-like or circle-like, comparing with the SS substrate (Fig. 4).

Furthermore, the platelet number on PTMCM-MOE3OM-*b*-PTMC, PTMC on PE substrate (Fig. 6a, b and 6c) were almost close or less than on SS substrate (Fig. 6d, e and 6f). Presumably, the polymer conformations on film surface were discrimination depending on substrate type and also affected to the platelet adhesion behavior. Besides, this result of the block copolymer PTMCM-MOE3OM-*b*-PTMC persuaded that the coating based on PE substrates was pretty better defensed the formation of blood clots compared to the SS substrates. Furthermore, the shapes of adhere platelets on PTMCM-MOE3OM-*b*-PTMC films resembled a spear-like (Fig. 5e and f) while the PTMC films arrayed the circle-like shapes (Fig. 5g and h). From the preliminary *in vitro* test, it is surmised that PTMCM-MOE3OM-b-PTMC has better potential to prevent clotting formation than PTMC.

4. Conclusion

The synthetic block copolymer, PTMCM-MOE3OM-*b*-PTMC using thermosensitive PTMCM-MOE3OM as a macroinitiator and TMC as comonomer, were achieved in order to improve the hydrophobicity for surface coating application. Thermal resistance profile (TGA) of the copolymer was showed at T_{10} = 206 °C, which was sufficient tendency for sterilization in clinical applications. Additionally, the stability of PTMCM-MOE3OM-*b*-PTMC dip coated films were investigated by

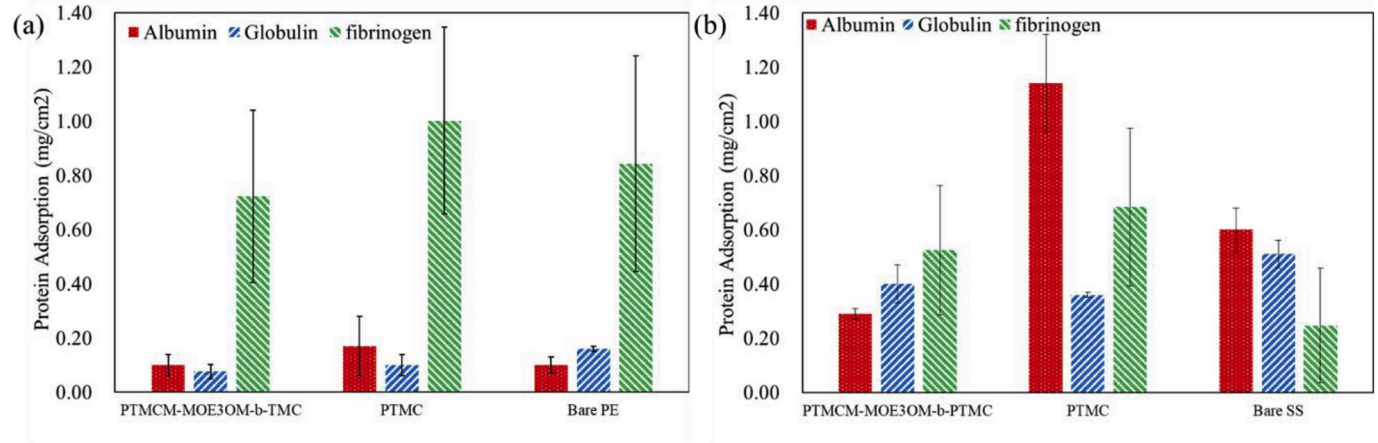


Fig. 3. (a) Protein adsorption to the PTMCM-MOE3OM-*b*-PTMC and the PTMC on the PE substrate and the PE. (b) Protein adsorption to the PTMCM-MOE3OM-*b*-PTMC and the PTMC on the SS substrate and the SS. Red bar: Albumin; Blue bar: Globulin; Green bar: Fibrinogen.

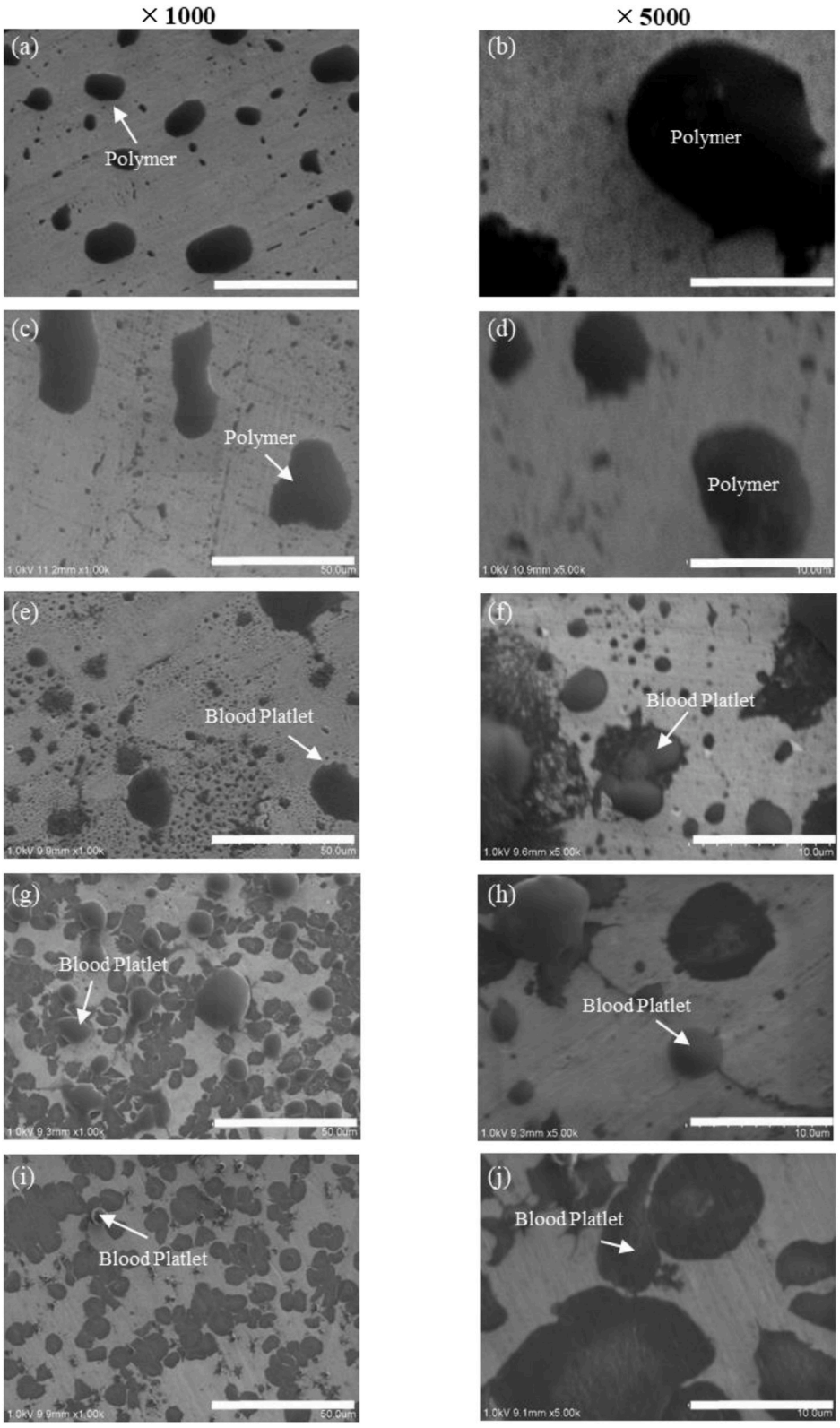


Fig. 4. SEM images of PTMCM-MOE3OM-*b*-PTMC-coated (a and b) and PTMC-coated (c and d) on SS. SEM images of adherent platelets on PTMCM-MOE3OM-*b*-PTMC-coated surfaces (e and f), PTMC-coated surface (g and h), and SS surface (i and j). (White bar indicates 10 μm)

peeling tests and the films were kept stable upon the physiological solution (PBS) for short on both SS and PE substrates. As previous researches, PTMCM-MOE3OM was appropriate to use *in vivo* conditions as biocompatible materials. Therefore, the bock copolymer films were examined both protein adsorption and platelet adhesion trial. Furthermore, the platelet adhesion properties of PTMCM-MOE3OM-*b*-PTMC films tended to prevent blood clot formation compared with PTMC films on both substrates. These results indicated that the design of ester free TMC derivatives are essential and play an important role for the development of low-toxicity coating materials. Our group hope this

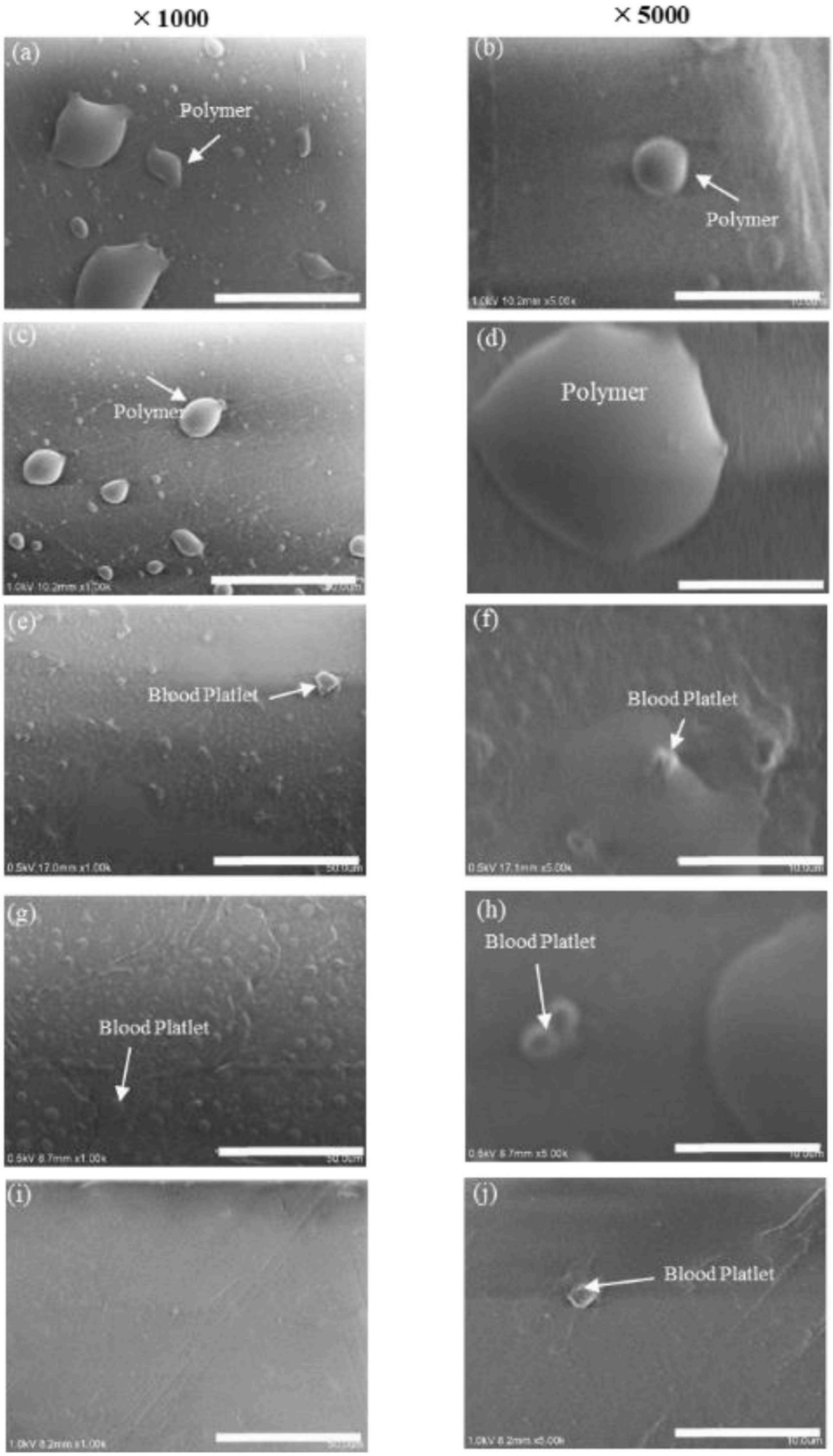


Fig. 5. SEM images of PTMCM-MOE3OM-*b*-PTMC-coated on PE (a and b) and PTMC-coated on PE (c and d). SEM images of adherent platelets on PTMCM-MOE3OM-*b*-PTMC-coated surfaces (e and f), PTMC-coated surface (g and h), and PE surface (i and j). (White bar indicates 50 μm ((a), (c), (e), (g), and (i)) and 10 μm ((b), (d), (f), (h), and (j)).

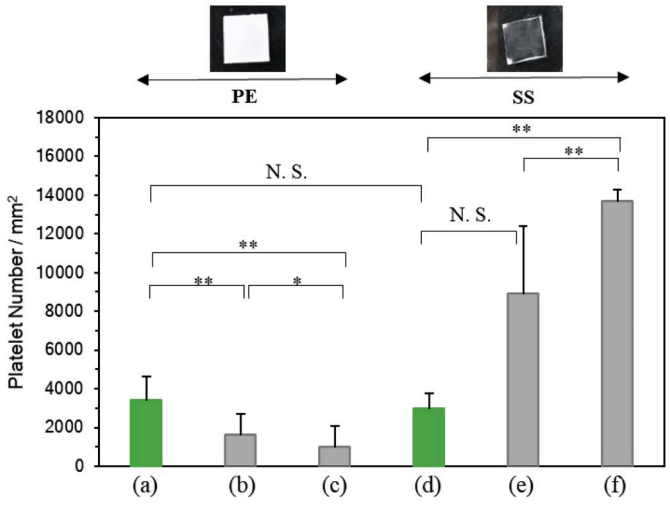


Fig. 6. Platelet adsorption to PTMCM-MOE3OM-*b*-PTMC on PE substrate (a), PTMC on PE substrate (b), PE (c), PTMCM-MOE3OM-*b*-PTMC on SS substrate (d), PTMC on SS substrate (e), and SS (f) (*p < 0.05, **p < 0.01. N. S. = Not Significant.).

film coating study will contributes to the consolidation of a road map for the molecular design of future developments.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Yoshiaki Haramiishi: Data curation, Writing - original draft. **Ryo Kawatani:** Visualization, Investigation, Software, Validation. **Nalinthip Chanthaset:** Software, Writing - review & editing. **Hiroharu Ajiro:** Conceptualization, Methodology, Software, Supervision, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.polymertesting.2020.106484.

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