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Shen-Guo Wang[a]; Chuan-Fu Chen[a]; Zhi-Fen Li[a]; Xue-Fen Li[a]; Han-Qing Gu[ab]
[a] Institute of Chemistry Academia Sinica, Beijing, China [b] Tianji Institute of Urologic Surgery, Tianjin, China

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MIXED POLYETHER-POLYESTER MULTIBLOCK COPOLYMER AND ITS BLOOD COMPATIBILITY

SHEN-GUO WANG,* CHUAN-FU CHEN, ZHI-FEN LI, XUE-FEN LI, and HAN-QING GU†

Institute of Chemistry
Academia Sinica
Beijing 100080, China

ABSTRACT

A new type of polyether-polyester block copolymer (MPEE) consisting of two components of polyethers (PTMGT and PEGT) as soft segment and one polyester (PET) as hard segment has been synthesized. It has also been investigated in comparison with blended polyether-polyester block copolymer (BPEE) consisting of the same composition ratio of hard and soft segments and both of the two polyethers (PTMG and PEG). It was found that 1) Improvement of blood compatibility of polyether-polyester block copolymer can be achieved by introducing the hydrophilic component PEG into it; 2) generally the blood compatibility of MPEE is better than that of BPEE; 3) at a specific molar ratio of PTMGT-PET to PEGT-PET (60/40), the blended copolymer (BPEE 60/40) shows the best blood compatibility, as well as the best mechanical properties. This might be related to smaller-size microphase-separated structures. The relationship between blood compatibility and structure of the copolymer is discussed. Polyether-polyester block copolymer containing hydrophilic and hydrophobic components might be a useful material with antithrombogenicity.

†Permanent address: Tianji Institute of Urologic Surgery, Tianjin, China.

INTRODUCTION

It is well known that the microheterophase structure of a polymeric material is an important factor in conferring good antithrombogenicity on it [1, 2]. It has also been reported that the ratio of hydrophilicity and hydrophobicity is closely correlated with the antithrombogenicity of the material [3-5]. Polyether-polyester block copolymer is one of the materials possessing a microphase-separated structure with excellent physicomechanical properties [6, 7]. It can be blended with other polymers, like silicone resin, to form biomaterials [8]. We have previously reported that the blood compatibility of of polyether-polyester block copolymer can be improved after grafting of acrylamide onto it, and the hydrophilicity of polymer was enhanced after grafting [9]. Although polyether-polyester block copolymer has been studied intensively as a thermoelastomer material, up to now there are only few reports concerning their biomedical properties, and there are no reports on synthesis and biomedical properties of polyether-polyester block copolymers consisting of the polyester as the hard segment and the mixed polyether with different hydrophilicities and hydrophobicities as the soft segment. In this paper a mixed polyether-polyester block copolymer, a new type of polyether-polyester block copolymer, consisting of two components as soft segments and one component as the hard segment, was synthesized, and its blood compatibility and the relationship between blood compatibility and structure were studied.

EXPERIMENTAL

Synthesis and Purification of Mixed Polyether-Polyester Block Copolymer

A mixture of polytetramethylene glycol (PTMG, MW 2200), polyethylene glycol (PEG, MW 2000), dimethyl terephthalate (DMT), ethylene glycol (EG), and tetrabutyl titanate catalyst ($Ti(OBu)_4$) were made to undergo an ester exchange reaction at 170-200°C for 1 h. Then the temperature was gradually raised to 250°C at 0.1 torr for 1 h. A mixed polyether-polyester block copolymer was obtained. The copolymer was purified by reprecipitation from chloroform solution with cold petroleum ether and then by extraction with ethanol for 10 h. Finally, it was dried at 40°C under vacuum for 10 h.

Determination of Copolymer Composition

The composition of the mixed polyether-polyester block copolymer was determined by ^{1}H NMR using a JOEL JNM-FX100 spectrometer with *d*-chloroform as solvent at room temperature.

Water Sorption

The water sorption of the copolymer was determined by the method reported before [10].

$$\text{Water sorption } (\%) = \frac{W_1 - W_2}{W_2} \times 100,$$

where W_1 is the weight of the copolymer after water sorption, and W_2 is the weight of the dried copolymer.

Mechanical Properties

Tensile strength and elongation of copolymer film cast from 8 wt% copolymer solution in chloroform were determined by an Instron 1122 at a stretching rate of 200 mm/min at room temperature.

Inherent Viscosity

The inherent viscosity of the copolymer at a concentration of 0.5 g/dL in *m*-cresol was determined at 30°C, and was calculated from η_r by the "One-Point Method" [11]:

$$[\eta] = \frac{\sqrt{2(\eta_{sp} - \ln \eta_r)}}{C},$$

and expressed in dL/g.

Contact Angle

Copolymer was dissolved in chloroform, and a copolymer film was obtained by casting the solution on a glass plate and evaporating the solvent at room temperature. After it was dried completely, the contact angle of the film to water was determined on the air surface of the film by a CA-D type contact-angle meter (Kyowa Kaimenkagaku Co.).

Blood Compatibility

1) Recalcification: A glass test tube was coated by copolymer. Then platelet-rich plasma (PRP) was added. After adding 25 m*M* aqueous calcium chloride solution, the test tube was shaken ($t = 0$). The time when a white precipitate formed was recorded as the recalcification time.

2) Platelet Sorption: This was measured by the improved Salzman Method [12] with Disposable Platelet Sorption Test Tubes using PRP, and was calculated by

$$\text{Platelet sorption } (\%) = \frac{N_0 - N}{N_0} \times 100,$$

where N_0 is the platelet number in the original PRP and N is the platelet number after the PRP was passed through the Platelet Sorption Test Tube.

Morphology of Polyether-Polyester Block Copolymer

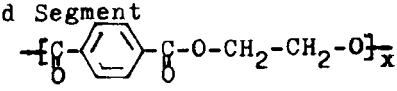
1) SEM samples were prepared by casting 8 wt% copolymer solution in chloroform on a glass plate, and evaporating the solvent slowly at room temperature for 4 h. Then the film surface was etched with an organic amine. The microphase-separated structure was observed with a Hitachi S-530 scanning electron microscope.

2) TEM samples were prepared by dropping 0.05 wt% copolymer solution in chloroform onto a copper screen. After the solvent had evaporated, the sample was dyed with ruthenium oxide, and the microdomain structure was observed with a Hitachi H-800 transmission electron microscope.

RESULTS AND DISCUSSION

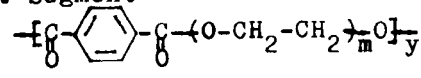
A series of mixed polyether-polyester block copolymers (MPEE) consisting of two components (PTMGT and PEGT) as the soft segment and one component (PET) as the hard segment was synthesized. Its structure is

Hard Segment

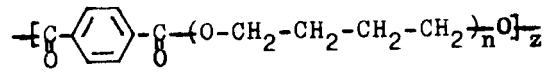


PET MW192

Soft Segment



PEGT MW2130



PTMGT MW2330

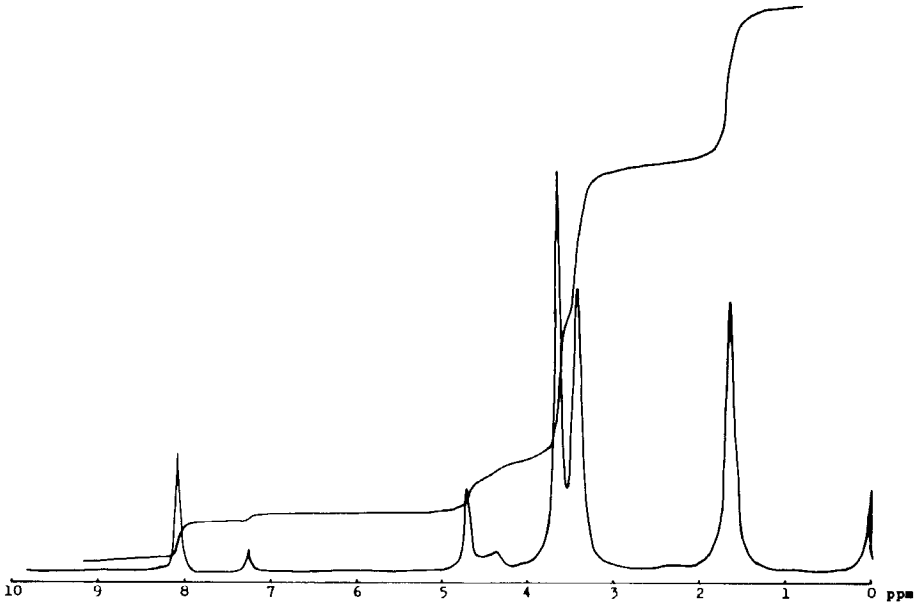


FIG. 1. ^{1}H-NMR spectrum of mixed polyether-polyester block copolymer in solution of $CDCl_3$.

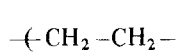
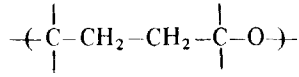
The composition of the copolymer was determined by ^{1}H NMR (see Fig. 1). The contents of each component in the copolymer can be calculated based on the chemical shifts of the various hydrogen atoms in the copolymer (see Table 1), and the composition of the copolymer (in molar ratio) can be calculated by

$$\text{(hard segment)/(soft segment)} = x/(y + z)$$

$$\text{PTMGT/PEGT} = z/y$$

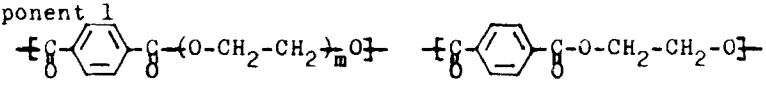
Table 2 shows that the composition of the copolymer calculated by ^{1}H NMR is in agreement with feed, i.e., the copolymer composition can be controlled by adjusting the feed ratio of two polyethers used. Water sorption, contact angle, mechanical properties, and blood compatibility of each MPEE copolymer were measured and compared with those of a blended polyether-polyester block copolymer (BPEE) of the same composition, i.e., ratio of hard to soft segment and of PTMGT to PEGT.

TABLE 1. ^{1}H NMR ($CDCl_3$) Chemical Shift

δ, ppm	Kind of hydrogen	Number of hydrogens[a]
8.09		$4x + 4y + 4z$
3.64		$4my$
1.62		$4nz$

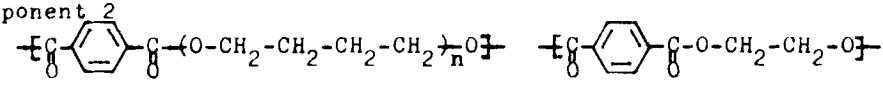
[a] $m = 45$, $n = 30$.

Component 1



PEGT MW2130 PET MW192

Component 2



PTMGT MW2330 PET MW192

It was found that the water sorption of both MPEE and BPEE increased with increasing PEGT content, and they have similar water sorption at the same PEGT content (Fig. 2). This means that the water sorption depends only on the overall ratio of the polyethers but is independent of the way in which they are combined (copolycondensation or blending). So the hydrophilicity and hydrophobicity of the products can be controlled by adjusting the ratio of the two polyethers (PTMG/PEG).

The blood compatibility is evaluated by testing for recalcification and platelet sorption. It was shown that the PEGT-PET type block copolymer possesses better blood compatibility than the PTMGT-PET type block copolymer (Table 3). This might be due to the higher water sorption of PEGT-PET, so that hydrophilicity/hydrophobicity appears to be one of the important factors affecting the blood compatibility of materials. A comparison of blood compatibility of MPEE with that of BPEE of the same composition is shown in Table 4. It was found that almost all of them had better blood compati-

TABLE 2. Dependence of Product Composition on Feed Composition

Molal ratio		T-5	T-6	T-7	T-8	T-9	T-2
Soft/Hard	Feed	22:78	22:78	22:78	22:78	22:78	22:78
	Product	22:78	23:77	23:77	20:80	22:78	23:77
PTMGT/PEGT	Feed	100:0	80:20	60:40	40:60	20:80	0:100
	Product	100:0	81:19	57:43	40:60	17:83	0:100

[a]PTMGT: Polytetramethylene glycol terephthalate. PEGT: Polyethylene glycol terephthalate.

bility than that reported for polyether urethane biomaterial [13]. On the other hand, generally MPEE has better blood compatibility than BPEE. Similar trends have been observed on polyurethane [14]. It should be pointed out, however, that unusual phenomena have been found in the blended copolymer with a molar ratio of PTMGT-PET to PEGT-PET of 60 to 40. Although its water sorption is not high (only 1/3.5 of that of PEGT-PET), it displays the best blood compatibility as well as higher inherent viscosity (Fig. 3), tensile strength, and elongation (Table 5) than other samples.

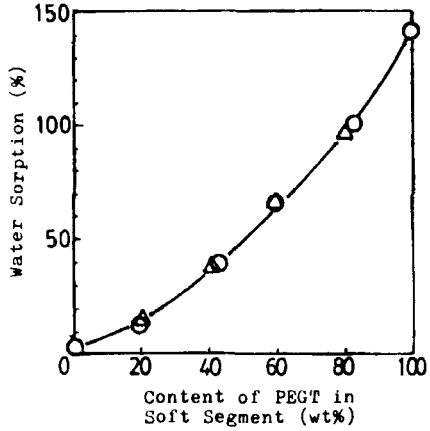


FIG. 2. Dependence of water sorption on PEGT content: (○) MPEE, (△) BPEE.

TABLE 3. Comparison of PEGT-PET Block Copolymer with PTMGT-PET Block Copolymer

	PEGT-PET	PTMGT-PET
Water sorption, wt%	140	0.8
Recalcification time, s	125	85
Platelet sorption, %	12.5	30

Contact angle results are shown in Fig. 4. There is no obvious difference among them, although composition and water sorption are different, possibly due to different distribution of each segment (ratio of oxygen to carbon) between the surface and the bulk of the samples. This will be reported in detail elsewhere [15].

The different microphase-separated structures observed in SEM photographs are shown in Fig. 5, where a bigger microphase-separated structure in BPEE (b) and a smaller microphase-separated structure in PTMGT-PET (a) can be seen. An even smaller surface structure was observed for BPEE (60/40) (c).

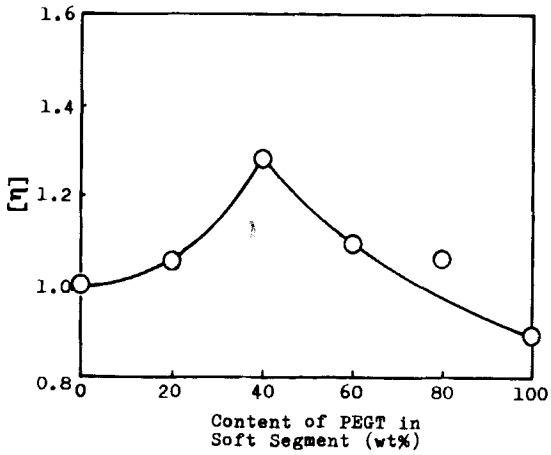


FIG. 3. Dependence of inherent viscosity of BPEE on composition (in *m*-cresol at 30°C).

TABLE 4. Blood Compatibility of MPEE and BPEE[a]

PTMGT/PEGT, mol ratio		100:0	80:20	60:40	40:60	20:80	0:100	PEU[b]
Recalcification time, s	MPEE	95	73	119	141	132	125	84
	BPEE		68	144	79	98		
Platelet sorption, %	MPEE	30	30	25	20	17.5	12.5	
	BPEE		25	12.5	22.5	22.5		

[a]MPEE: Mixed polyether-polyester block copolymer. BPEE: Blend of polyether-polyester block copolymers.
[b]PEU: One kind of polyether urethane [13].

TABLE 5. Dependence of Mechanical Properties on the Composition of BPEE

	T-5	T-16	T-17	T-18	T-19	T-2
PTMGT/PEGT	100:0	80:20	60:40	40:60	20:80	0:100
Tensile strength, kg/cm^2	1.84	1.51	1.60	1.34	1.30	1.31
Elongation, %	900	652	915	767	637	554

TEM photographs show that all kinds of polyether-polyester block copolymers possess a microphase-separated structure, but that the dimensions of the microdomains in BPEE (60/40) are much smaller than those of the other samples (Fig. 6). This suggests that the smallest microphase-separated structure leads to better blood compatibility.

The best compatibility between the two components (PTMGT-PET and PEGT-PET) appears to exist at this component ratio. The microdomain of BPEE (60/40) (about 50 Å) is therefore suitable for blood-compatible structure (Fig. 7).

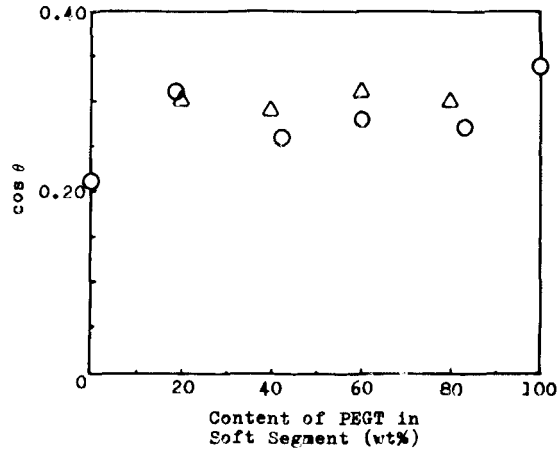


FIG. 4. Dependence of contact angle on the composition of copolymers: (○) MPEE, (△) BPEE.

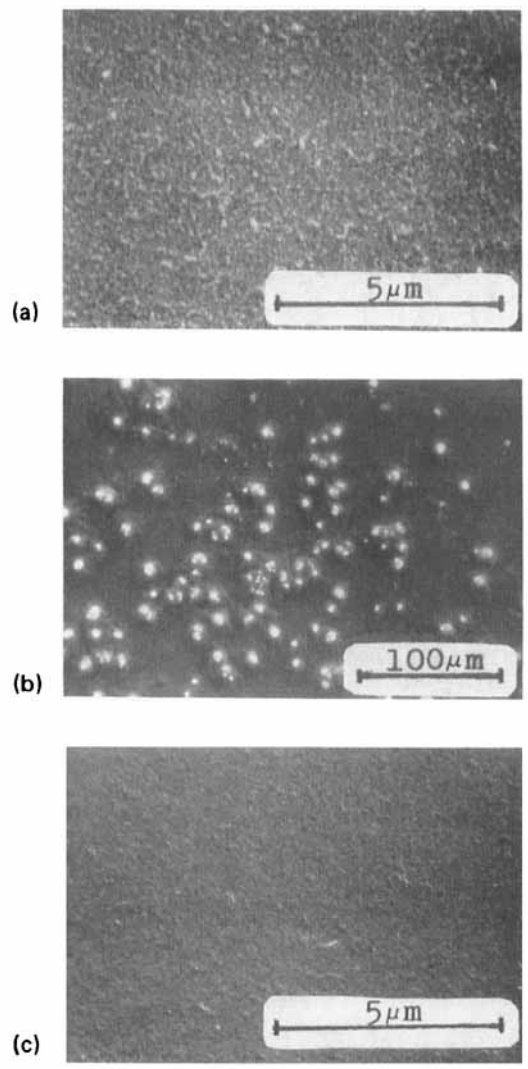


FIG. 5. SEM photographs of PTMGT-PET copolymer and BPEE copolymers: (a) PTMGT-PET copolymer, (b) BPEE copolymer, (c) BPEE copolymer (60/40).

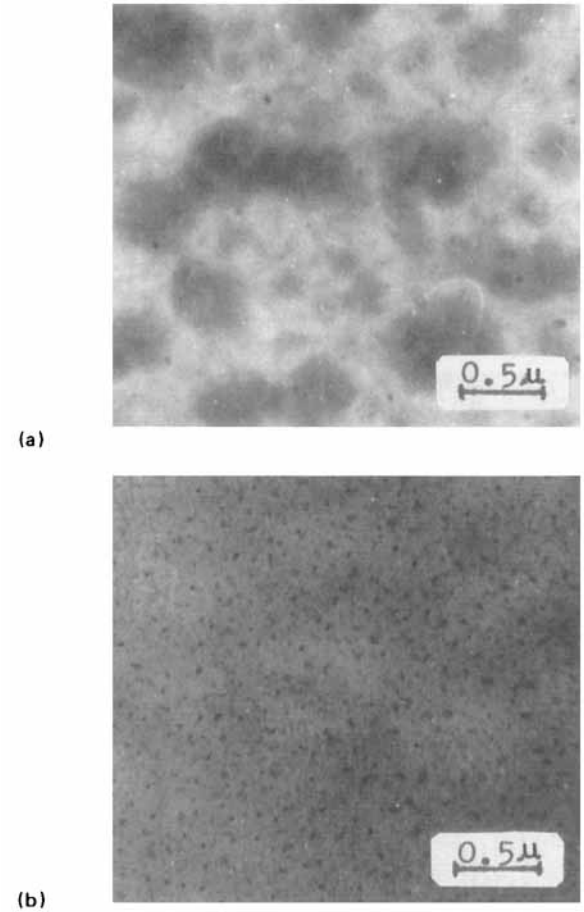


FIG. 6. TEM photographs of microphase-separated structure of PEGT-PET (a) and BPEE (60/40) (b).

It was concluded that: 1) Improvement of antithrombogenicity of polyether-polyester block copolymer can be achieved by introducing hydrophilic PEG into it; 2) generally, the blood compatibility of a mixed polyether-polyester block copolymer (MPEE) is better than that of the corresponding blended one (BPEE); 3) but at a specific molar ratio of PTMGT-PET to

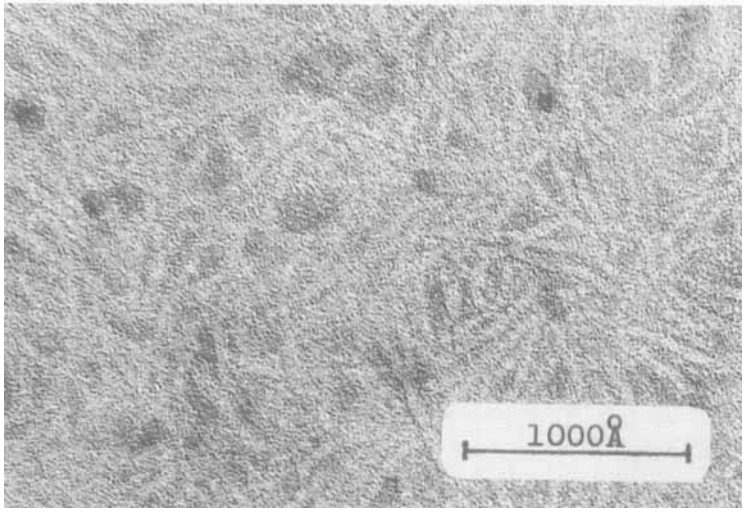


FIG. 7. TEM photograph of microphase-separated structure of BPEE (60/40).

PEGT-PET (60/40), the blended copolymer shows the best blood compatibility, as well as better mechanical properties. This might be related to its smaller microphase-separated structure.

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