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Biocompatible Polyamides and Polyurethanes Containing Phospholipid Moiety

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1. Introduction

The non-thrombogenic biomaterial has been received a great interest for the development of medical devices or implants in these few decades. When any medical device contacts with flowing blood or internal organs, the material surface of device should avoid the initiation of the process leading to a thrombosis. Such a biocompatible property of artificial biomaterials is a very important factor to use the materials for long-term implantable devices, extracorporeal circulation and intravenous catheters sensors. Although a lot of medical devices are used clinically, the universal non-thrombogenic material has not yet been developed and these devices have been limited to be used for long-term implantation. On the other hand, phospholipids are the main components of cell membranes and act as interesting substances in biological and biomedical fields (Chapman, 1968; Gregoriadis & Allison, 1980; Hayward & Chapman, 1984). Several attempts have been made to translate the natural compatibility between blood and phospholipid membranes for the application of medical devices. The phosphorylcholine (PC) group is a polar component of phospholipid molecules, which covers the surface of cell membranes. It has been well known that synthetic polymer materials containing PC group exhibit biocompatibility including blood compatibility (Sugiyama *et al.*, 1995; Ohishi *et al.*, 1997; Gong *et al.*, 2005). Especially, the so-called MPC polymer, which is typically a copolymer of 2-methacryloyloxyethyl phosphorylcholine (MPC) with butyl methacrylate, has been reported as ideal non-thrombogenic and excellent biocompatible materials (Ishihara *et al.*, 1990a, 1990b, 1991; Ueda *et al.*, 1992). This polymer was designed based on the inspiration from the outer surface of the cell membrane, *i.e.* the biomembrane, which is mainly constructed of natural phospholipid molecules. In particular, the adhesion and the activation of platelets were completely suppressed on the surface of the MPC polymer, and the amount of plasma proteins adsorbed on the surface of MPC polymer film was clearly decreased. Since PC group consists of a zwitterion, MPC polymer behaves as an entire neutrality molecule and exhibited no interaction with specific ions in the living organism. Furthermore, the applications to medical devices and other uses have been greatly advanced in these years (Sawada *et al.*, 2006; Patel *et al.*, 2005; Iwasaki *et al.*, 1997; Uchiyama *et al.*, 2002; Ye *et al.*, 2006; Goda & Ishihara, 2006; Snyder *et al.*, 2007). Therefore, MPC polymers are useful polymeric biomaterials not only in the biomedical field but also in the tissue engineering and bioengineering fields.

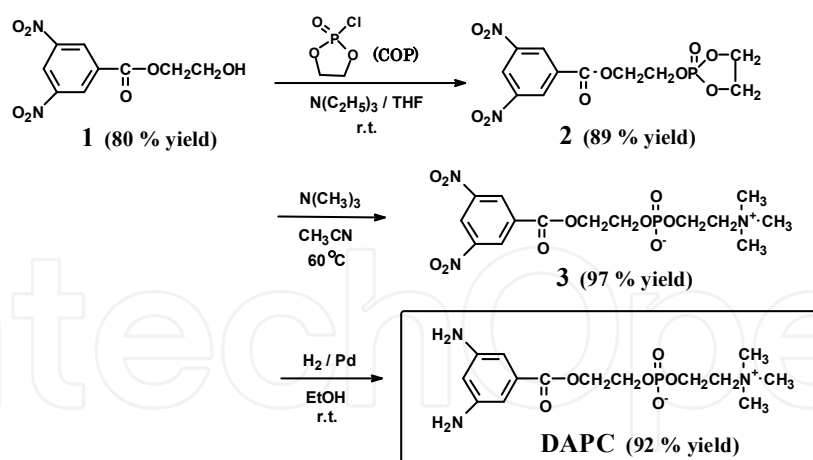
However, most of MPC polymers do not possess the enough durability to several solvents such as alcohols, the thermal stability and the mechanical strength, which were derived from the polymethacrylate type main chain structure. Then, if these physical properties of MPC polymers improved satisfactorily while maintaining the excellent biocompatibility, novel biocompatible polymer materials could be developed. Recently, we have succeeded in synthesizing a novel diamine monomer containing PC moiety and preparing aromatic polyamides and poly(urethane-urea)s from the monomer (Nagase *et al.*, 2007, 2008; Horiguchi *et al.*, 2008). In addition, PC group was also introduced into ethyl cellulose by polymer reaction using carboxylic compound containing PC group (Tadokoro *et al.*, 2007). It was found that the obtained polymers exhibited the excellent biocompatibility derived from PC unit in addition to the processability, the durability to solvents, the thermal stability and the mechanical strength, which were derived from the main chain components.

In this chapter, the synthetic pathway of novel aromatic diamine monomers containing PC moiety will be described at first. Then, we will describe the preparations of high molecular weight aromatic polyamides and poly(urethane-urea)s containing PC group, which are obtained by polycondensation and polyaddition using these monomers. Furthermore, the physical properties such as solubility, thermal property, biological function as blood compatibility, and surface property of the obtained polyamides will be discussed to reveal the possibility of a durable biocompatible polymer material.

2. Diamine monomer containing phospholipid moiety

At first, our history of development of novel aromatic diamine compound will be described. The synthetic route of the diamine monomer containing PC group, 2-(3,5-diaminophenylcarbonyloxy)ethyl phosphorylcholine (DAPC), is shown in Scheme 1. The starting material, a dinitro compound (**1**), was prepared by the reaction of 3,5-dinitrobenzoyl chloride with excess amount of ethylene glycol in good yield. Then, the reaction of **1** with 2-chloro-2-oxo-1,3,2-dioxaphospholane (COP) yielded a phospholane compound (**2**), which was an intermediate of phosphorylcholine compound. The purification of **2** by a silica-gel column chromatography was difficult because it was easily hydrolyzed. However, the extraction of the crude products with chloroform followed by washing with distilled water gave the pure product of **2**. Next, DAPC was obtained by opening the cyclic phosphoric ester moiety of **2** with trimethylamine, followed by the reduction of the nitro groups of **3** with H₂ catalyzed by Pd. The chemical structure of DAPC was confirmed by IR and ¹H-NMR spectra. In the IR spectra of DAPC, a broad adsorption peak in the region of 3400-3150 cm⁻¹ was observed as the amino groups, and the PC group was identified by the peak at 1228 and 1076 cm⁻¹. This aromatic diamine compound, DAPC, would be a useful monomer for the syntheses of various aromatic polymers, such as polyamides, polyimides, polyureas and poly(urethane-urea)s that have PC group in the side chain.

Next, the synthesis of copolyamide was carried out by the polycondensation of DAPC with isophthaloyl chloride and another diamine comonomer. As the comonomer, 4,4'-diamino-3,3'-dimethyldiphenylmethane was used to make the polymer soluble in some solvents. Namely, the aromatic copolyamides containing PC group could be successfully prepared from DAPC, whose composition of DAPC unit was 21 mol%. A homopolyamide without PC group was prepared from 4,4'-diamino-3,3'-dimethyldiphenylmethane and isophthaloyl chloride to compare the biocompatible properties with PC-containing copolyamide.



Scheme 1. Synthesis of diamine monomer containing PC moiety (DAPC).

The thin films of these polyamides were prepared by coating of the NMP solutions of the polymers on poly(ethylene terephthalate) (PET) plates, and the blood compatibility of the coating films was evaluated by contacting the coated plates with a human blood. Fig. 1 shows SEM pictures of the two film surfaces of PC-containing copolyamide and homopolyamide without PC unit after contact with human platelet-rich plasma (PRP) for 60 min. The numerous adherent platelets on the homopolyamide surface were observed as large aggregates. In contrast, the platelets were significantly suppressed on the copolyamide film surfaces as shown in Fig. 1(a). These results clearly indicated that PC-containing copolyamide exhibited the excellent blood compatibility and PC unit in the copolyamide was an important element to develop the blood compatibility. Furthermore, the composition of the PC unit was a dominant factor in the reduction of the platelet adhesion (Nagase *et al.*, 2007). These results would be due to the PC unit located at the surface of the polymer film, where the surface is covered with PC unit, and the interaction between the polymer surface and blood ingredients such as cells and platelets is very weak.

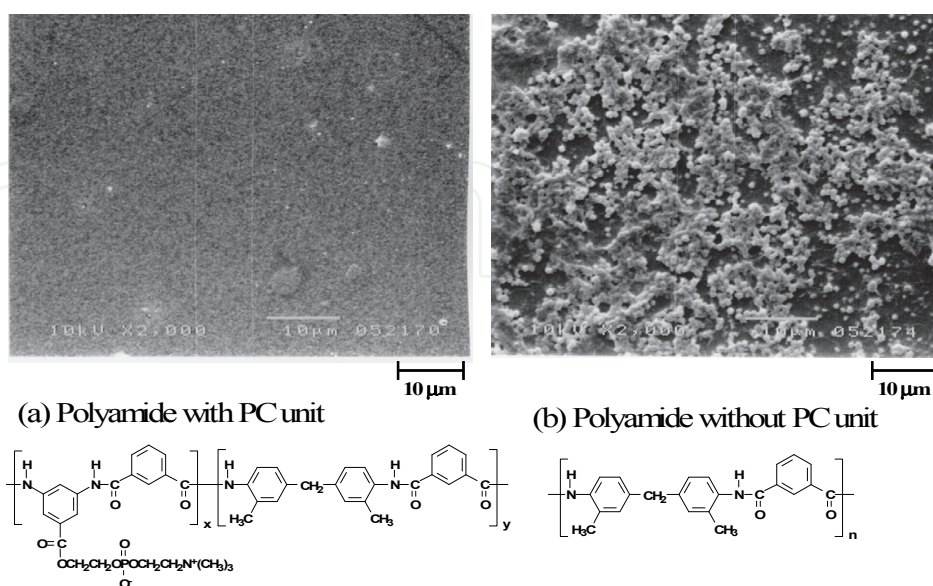
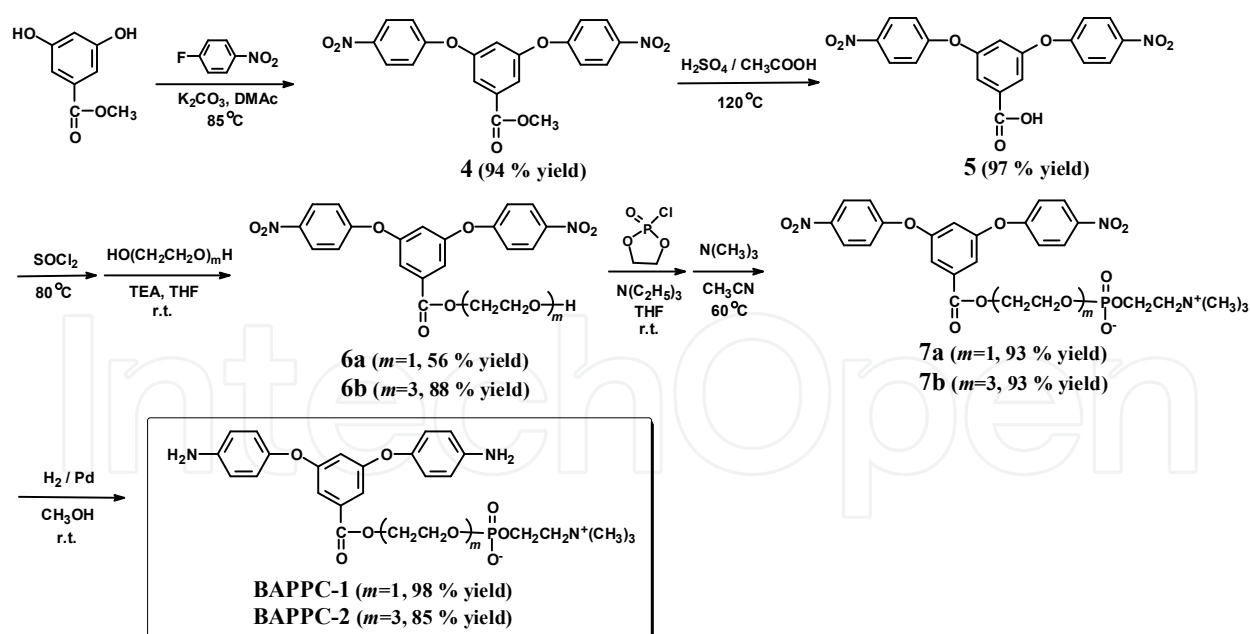


Fig. 1. SEM pictures of polyamide film surfaces with and without PC unit after contact with human PRP for 60 min at $37^\circ C$. ($\times 2,000$)

However, the molecular weight and the PC content of copolyamides from DAPC were not enough to produce a self-standing film and to exhibit the higher biocompatibility, respectively, which would be due to the low reactivity and also the highly hygroscopic property of DAPC. Thus, we have projected a new structure of high molecular weight polymer in order to create the practical biomaterials for several applications, which exhibit the excellent biocompatibility in addition to the processability, the durability to solvents, the thermal stability and the mechanical strength. For this purpose, we designed a new diamine monomer containing PC group, 2-[3,5-bis(4-aminophenoxy)phenylcarbonyloxy]ethyl phosphorylcholine (BAPPC in Scheme 2), to solve these problems of DAPC. BAPPC is expected to show the higher reactivity in the polymerization than DAPC, which would be due to the relatively higher reactive amino groups on *p*-position of phenoxy groups.

The synthetic route of the new PC-containing diamine monomer is outlined in Scheme 2. Two kinds of monomers were prepared, which have the different spacer structures between 3,5-bis(4-aminophenoxy)phenyl and PC groups. If the longer and flexible spacer could be introduced into the monomer structure, it is expected that the PC group in the polymer would be easily oriented on the surface because of the mobility of flexible spacer. Then, two compounds, **6a** and **6b**, were prepared as intermediates, which were obtained by the esterification of **5** with ethylene glycol and tri(ethylene glycol), respectively. From **6a** and **6b**, the two diamine monomers, BAPPC-1 and 2, were prepared according to the same pathway as the preparation of DAPC in Scheme 1. Although the several reaction steps are necessary to prepare these monomers, all of the reaction steps proceeded smoothly in high yields. This novel diamine monomers, BAPPC-1 and 2, would be useful for the synthesis of various aromatic polymers which has PC group in the side chain.



Scheme 2. Synthesis of diamine monomers containing PC moiety (BAPPC).

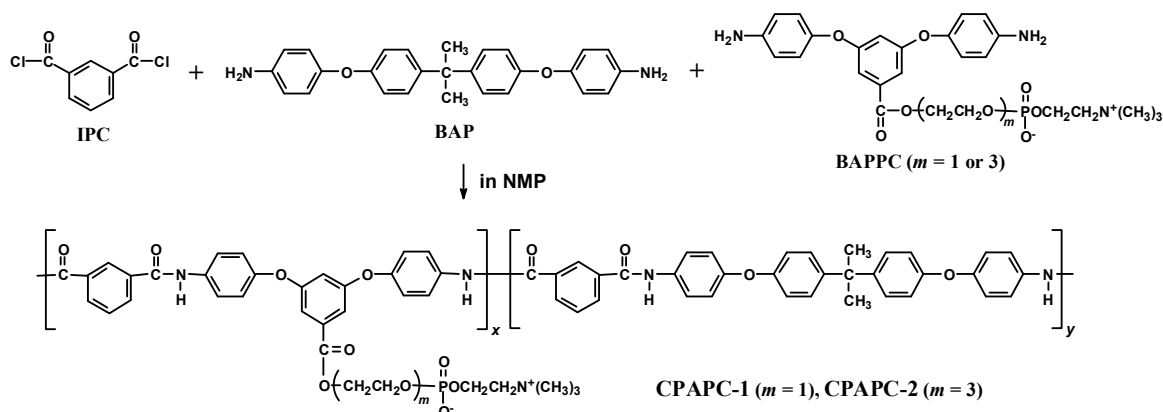
3. Aromatic polyamides containing phospholipid moiety

In general, the aromatic polyamides are insoluble in many solvents, thermally stable up to $300^\circ C$ and mechanically tough materials, which are used in a lot of electric devices and

motorcars. Therefore, we attempted to prepare aromatic polyamides containing PC group in the side chain by using the PC-containing diamine monomers, which would lead to new biocompatible polyamides derived from the characteristics of phospholipid moiety.

3.1 Preparation

The preparations of copolyamides were carried out by the polycondensations of BAPPC-1 or 2 with isophthaloyl chloride and another diamine comonomer, as shown in Scheme 3. As the comonomer, 2,2-Bis[4-(amino-phenyloxy)phenyl]propane (BAP) was used to make the polymer soluble in some solvents. On the other hand, a polyamide without PC group (PA) was prepared from BAP and isophthaloyl chloride to compare the physical property with PC-containing copolyamides. Table 1 summarizes the results of polymerizations. Eight kinds of copolyamides with different spacer structures and contents of PC unit were prepared by changing the ratio of monomers in the feed of polymerization. The obtained copolyamides had the number-average molecular weights (M_n) more than 10^5 , while the M_n of polyamides prepared from DAPC in Scheme 1 was in the order of $10^3 - 10^4$. Therefore, it is suggested that this novel diamine monomer containing PC group has high reactivity in the polymerization, and would be useful for the preparations of other high molecular weight polymers such as polyimide and polyurea containing PC group.



Scheme 3. Preparation of copolyamide containing PC moiety (CPAPC).

Code	m	Composition (mol%)		M_n^b ($\times 10^4$)	M_w/M_n^b
		BAPPC/BAP	x/y^a		
CPAPC-1a	1	30/70	24/76	18.2	4.03
CPAPC-1b	1	50/50	46/54	57.9	2.01
CPAPC-1c	1	70/30	54/46	59.1	2.05
CPAPC-1d	1	100/0	100/0	--	--
CPAPC-2a	3	30/70	28/72	11.3	3.21
CPAPC-2b	3	50/50	45/55	22.8	3.14
CPAPC-2c	3	70/30	57/43	24.9	3.31
CPAPC-2d	3	100/0	100/0	36.0	2.06
PA	--	0/100	0/100	49.0	2.34

a) The copolymer composition, x/y , was determined by $^1\text{H-NMR}$.

b) Number-average and weight-average molecular weights (M_n and M_w) were estimated by gel permeation chromatography using DMF as eluent.

Table 1. Results of polycondensations.

These copolyamides were soluble in aprotic polar solvents, such as dimethylformamide (DMF), dimethylsulfoxide (DMSO) and *N*-methyl-2-pyrrolidinone (NMP), at room temperature, whereas they were insoluble in water, methanol, ethanol, acetone and other ordinary organic solvents. This solubility in specific solvents is advantageous in the processing for medical devices, and the insolubility in other solvents enables the material durable. On the other hand, PC-containing homopolyamides, CPAPC-1d and CPAPC-2d in Table 1, exhibited the less solubility than the copolyamides. For example, CPAPC-1d was insoluble in DMF, therefore, the gel permeation chromatography to determine the molecular weight could not be measured. It is considered that such homopolyamides with high content of PC unit has a strong molecular interaction between polar PC group and amide bond or other PC group to make the polymer insoluble in solvents. Therefore, the copolymerization of BAPPC with other diamine monomer would be effective to obtain soluble and processable polymer material.

3.2 Biocompatibility

The blood compatibility of the copolyamide was evaluated by contacting the copolyamide films with human blood. Circular pieces of PET plates (diameter: 14 mm, thickness: 0.2 mm) were dipped in polymer solutions in NMP for 30 min, and the obtained polymer-coated PET plates were dried. Then, the homogeneous coating films on PET plates were prepared from CPAPC-2 series and other polymers. The polymer-coated PET plates were contacted with phosphate-buffered solution (PBS, pH=7.4) at r.t. for overnight to equilibrate the surface, then human whole blood or PRP was poured onto the plates and incubated for 60 min at 37°C. After the incubation, whole blood and platelet-rich plasma (PRP) were removed with an aspirator, and the plates were rinsed three times with PBS, and then 0.7 ml of 2.5 vol.% glutaraldehyde in PBS was poured onto each plate, and the materials were maintained at room temperature for 2 h in order to fix the blood components on the plates. After the fixation, it had been rinsed five times with distilled water, and then the plate was freeze-dried. The surfaces of the polymer-coated plates were observed with a scanning electron microscope (SEM), and the number of adhered platelets was estimated by the procedure written in our literature (Nagase *et al.*, 2007).

Fig. 2 shows the SEM pictures of PA and CPAPC-2c and 2d film surfaces after contact with PRP. As seen in this figure, it was clarified that the large aggregates of the human platelets occurred on polyamide (PA) film, where a lot of adhered platelets were observed. On the contrary, PC-containing copolyamide films resisted the adhesion of platelets.

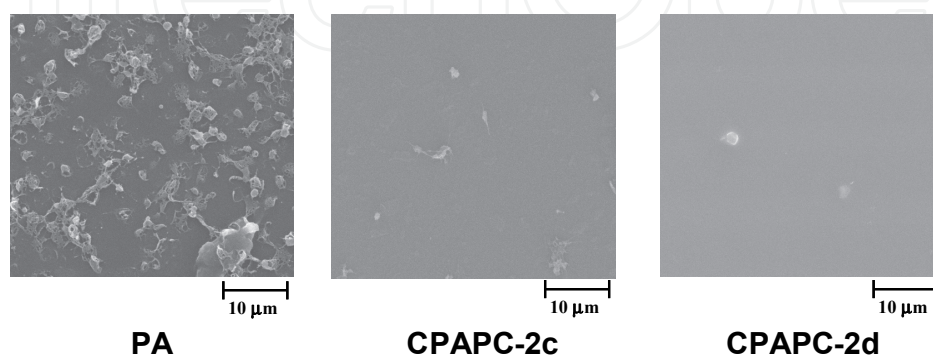


Fig. 2. SEM pictures of polyamide film surfaces with and without PC unit after contact with human PRP. ($\times 2,000$)

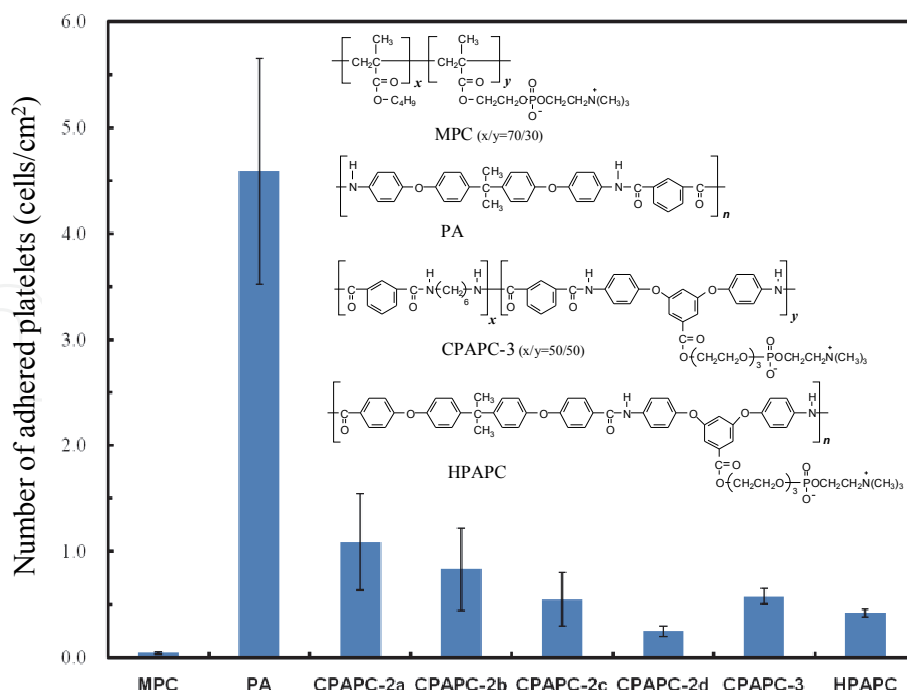


Fig. 3. Number of adhered platelets on the polymer films after contact with human PRP for 1 h.

The quantitative analysis of adhered platelets of each polymer film was also carried out to reveal the strict difference of thrombogenic property of these polymer films. Fig. 3 represents the difference of the number of platelets that adhered on each coated film. In this figure, the data of MPC polymer and other kinds of PC-containing polyamides, CPAPC-3 and HPAPC, are included to compare with PA and CPAPC-2 series. CPAPC-3 is a similar copolymer to CPAPC-2 series, the comonomer of which is 1,6-diaminohexane instead of BAP. HPAPC is a homopolyamide obtained from the polycondensation of BAPPC-2 with 4,4'-(4-carboxylphenoxy)-2,2-diphenylpropane, which has a good solubility in aprotic polar solvents. MPC polymer coated film has been also evaluated, because it is a good reference as the very high biocompatible material.

As shown in Fig. 3, it was obvious that PC-containing polyamides efficiently reduced the adhered platelets than polyamide without PC group (PA), where the number of adhered platelets of these polyamides was reduced in nearly one-tenth amount as compared with that of PA. These results indicate that the PC unit plays an important role for the blood compatibility of the polymers. Furthermore, the amount of adhered platelets decreased as the increase of the content of PC unit in CPAPC-2 series, therefore, the composition of the PC unit was a dominant factor in the reduction of the blood cell and platelet adhesion. For example, the amount of adhered platelets of CPAPC-2a (PC content: 28 mol%) was ten times larger than that of CPAPC-2d (PC content: 100 mol%). The similar tendency was observed for CPAPC-1 series (Horiguchi *et al.*, 2008). Therefore, the difference of the spacer structure of these copolyamides would not affect the biocompatibility. On the other hand, MPC polymer exhibited the extremely high nonthrombogenicity among the polymers evaluated in Fig. 3. Consequently, the improvement of nonthrombogenicity by introducing PC unit in such polyamide system would be limited, although the phospholipid moiety is effective to considerable extent for the reduction of the platelet and protein adhesion.

3.3 Physical property

The thermal property of PC-containing polyamides was evaluated by differential scanning calorimetry (DSC) and thermogravimetric analysis (TGA). The glass transition temperature (T_g) and the melting temperature (T_m) were not observed for CPAPC-1 and 2 series in the range between -100°C and 250°C of DSC thermograms, which suggested that these polyamides were glassy polymers. In general, aromatic polyamides are known to exhibit a crystalline state, however, bulky PC group in the side chain would prevent the crystallization of polyamide backbone.

Fig. 4 shows the TGA curves of PA and CPAPC-1b and 2b under N_2 flow. As seen in this figure, the thermal degradation of homopolyamide, PA, started at about 400°C , but the PC-containing copolyamides degraded at about 250°C . This would be due to the thermal degradation of polymer side chain, which consisted of the PC or spacer moiety. In nitrogen atmosphere, the aromatic backbone would be carbonized, which resulted in the residue more than 30 % at 1000°C . In the case of the copolyamides, the phosphate moiety would be incombustible, where the residue was a little higher, nearly 50 %. Anyhow, the heat resistance of these PC-containing polyamides until 250°C is enough to use for biomaterial devices, for example, for the thermal sterilization process over 150°C .

The very tough films could be obtained from PC-containing copolyamides by solvent casting method. Then, the mechanical properties of these copolyamides and MPC polymer films were quite different, where Young's moduli of the copolyamides, PA and MPC polymer films were 200-400, 642 and 15.2 MPa, respectively. Therefore, the physical properties of PC-containing copolyamides obviously depended on the aromatic polyamide backbone. Consequently, it is expected that the aromatic copolyamides containing PC group will be useful polymeric biomaterials to develop a new generation of biomedical devices, because of the durability to solvents, the high thermal stability and mechanical strength in addition to the good biocompatibility.

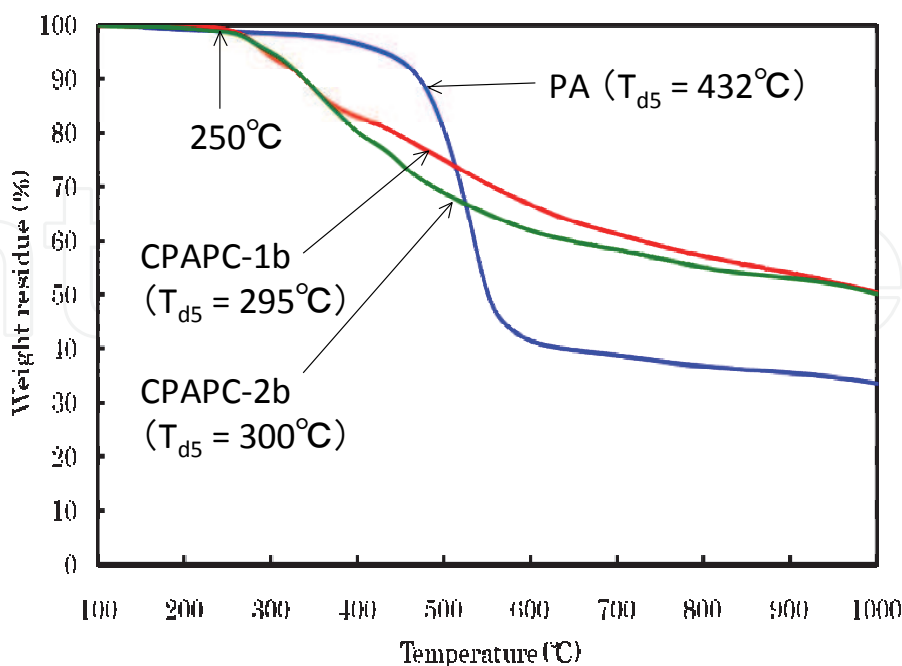


Fig. 4. TGA curves of polyamides at heating rate of $10^\circ\text{C}/\text{min}$ in N_2 flow.

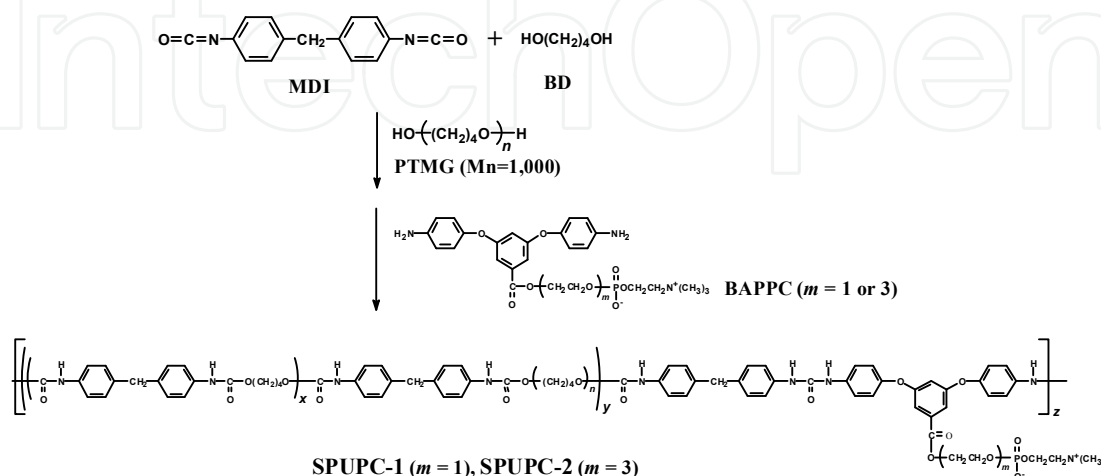
4. Segmented poly(urethane-urea) containing phospholipid moiety

Segmented polyurethanes have been widely used in the practical medical devices as elastomers (Lelah, 1986; Eisenbach, 1996) because of their suitable mechanical properties and biocompatibility, which consisted of short alternating blocks of soft and hard segments. The soft segment is typically a low glass transition temperature (T_g) polyether, polyester or polycarbonate, the molecular weights of which are 400-2000. The hard segment is usually a high T_g component, such as semicrystalline aromatic diisocyanate linked with a low molecular weight chain extender. The biocompatibility of segmented polyurethane is thought to be derived from the micro phase separation of soft and hard segments. However, the blood compatibility of segmented polyurethane is not enough to be applied for long-term implantation. It has been suggested that the biodegradation and cracking of polyurethane occurred *in vivo* due to the adsorption of proteins, the adhesion of macrophages and the peroxide formation (Zao *et al.*, 1991, 1993; Wu *et al.*, 1991), which resulted in the reduction of the mechanical strength of SPU. Moreover, it was reported that the soft segment of segmented polyurethane was degraded by the oxygen radicals produced from adherent macrophages (Stokes *et al.*, 1995). Therefore, several studies of the surface or chemical modification of segmented polyurethanes have been conducted to improve the blood compatibility through reducing the adhesion of cells and proteins (Kang *et al.*, 1997; Flemming *et al.*, 1999; Mathur *et al.*, 1997; Roh *et al.*, 1999; Lee *et al.*, 2000). The composite material of segmented polyurethane and MPC polymer has been also reported, which showed the high biocompatibility and the elasticity (Ishihara *et al.*, 2000).

In our study, as another approach to improve the biocompatibility of segmented polyurethane which has been widely used as a biomedical material, we attempted to prepare segmented poly(urethane-urea) containing PC group by using the PC-containing diamine monomer as a coupling reagent in the polyaddition of diols with diisocyanate, which was expected as new biocompatible polymers by combining the characteristics of segmented polyurethane and phospholipid moiety.

4.1 Preparation

As shown in Scheme 3, segmented polyurethane was first prepared by polyaddition of 4,4'-diphenylmethane diisocyanate (MDI) with 1,4-butanediol (BD) in NMP, followed by the addition of hydroxyl-terminated poly(tetramethylene glycol) (PTMG) as the soft segment.



Scheme 3. Preparation of segmented poly(urethane-urea) containing PC moiety (SPUPC).

Next, in the polymerization vessel, PC-containing diamine monomer, BAPPC-1 or 2, was added to couple the polyurethane to obtain segmented poly(urethane-urea)s containing PC unit (SPUUPC-1 and 2). These polymerization reactions proceeded smoothly without catalyst. By the way, dibutyltin dilaurate was necessary as a catalyst for the preparation of the similar segmented poly(urethane-urea) using DAPC in Scheme 1 (Nagase, *et al.*, 2008).

Table 2 summarizes the results of polymerizations. A few poly(urethane-urea)s with different contents of PC unit were prepared by changing the amount of BD, PTMG and BAPPC-1 or 2 in the polyaddition. The chemical structures of these polymers were confirmed by their ¹H-NMR and IR spectra. The compositions of PC unit in these copolymers were determined from the ratio of the peak intensities of the ammonium protons (3.10 - 3.15 ppm) of PC unit and methylene proton (3.78 - 3.80 ppm) of *p,p'*-diphenylmethane unit, which existed in every monomer components. In the gel permeation chromatography, bimodal peaks were observed in most of these copolymers. Thus, each two values were listed in Table 2 as the number-average molecular weights (*M_n*) of the obtained copolymers, which were in the range of 10⁴ and 10⁶. Probably, the higher molecular weight segments over 10⁶ would be partly produced in the final coupling reaction with BAPPC-1 or 2. Anyhow, very high molecular weight poly(urethane-urea)s containing phospholipid moiety have been successfully prepared by polyaddition with PC-containing diamine monomers.

Code	<i>m</i>	BD/PTMG/BAPPC ^a)	PC content		<i>M_n</i> ^b)	
			(mol%)	(wt.%)	(x10 ⁴)	<i>M_w/M_n</i> ^b)
SPUUPC-1a	1	50 / 33 / 17	14	2.5	1.86	1.88
SPUUPC-1b	1	33 / 34 / 33	27	9.1	7.47, 254	1.85, 1.03
SPUUPC-1c	1	17 / 33 / 50	47	22	1.35, 99.0	1.78, 1.87
SPUUPC-2a	3	50 / 33 / 17	15	6.3	2.19, 210	1.74, 1.15
SPUUPC-2b	3	33 / 34 / 33	28	13	2.01, 120	1.51, 1.57
SPUUPC-2c	3	17 / 33 / 50	49	25	2.19, 111	1.82, 1.47
SPU	--	67 / 33 / 0	0	0	2.62	1.46

a) The molar ratio of monomers in the polyaddition.

b) Number-average and weight-average molecular weights (*M_n* and *M_w*) were estimated by gel permeation chromatography using DMF as eluent.

Table 2. Results of polyadditions.

The obtained poly(urethane-urea)s exhibited a good solubility in aprotic polar solvents such as NMP, DMF and DMSO at room temperature, whereas it was insoluble in methanol, ethanol, acetone, chloroform and water. Such solubility in the specific solvents is advantageous in the processing for medical devices, and the insolubility in other solvents enables the material durable to these solvents. Actually, flexible and self-standing films could be prepared from these copolymers by a solvent casting method.

4.2 Biocompatibility

The blood compatibility of the poly(urethane-urea) films was evaluated by the similar procedure described in Section 3.2. For this experiment, the self-standing films prepared from each copolymer were used, not coating film. Fig. 5 shows the number of platelets adhered on the polymer films after contact with PRP for 1 h. It was found that the platelet adhesion was suppressed to a certain extent even on SPU film without PC unit, where the

amount of adhered platelets was quite different from the values of polyamide (PA) shown in Fig. 3. Therefore, segmented polyurethane would have the higher non-thrombogenic efficiency than aromatic polyamide and other normal polymer materials. Furthermore, PC-containing poly(urethane-urea)s, SPUPC-2b and SPUPC-2c, efficiently reduced the platelet adhesion rather than SPU, and the number of adhered platelets of these copolymer films were almost same as that of MPC polymer film. Furthermore, the composition of PC unit was a dominant factor in the reduction of the blood cell and platelet adhesion, which was revealed from the result that the number of adhered platelets was much decreased on SPUPC-2c film rather than SPUPC-2a and SPUPC-2b films. Thus, the PC content of 25 wt.% in SPUPC-2c would be necessary to sufficiently reduce the platelet adhesion on the polymer surfaces, which would be an enough content of the PC unit located at the surface of the polymer film. The surface chemical structure of SPUPC-2c film was analyzed by X-ray photoelectron spectroscopy (XPS). The XPS signals was observed at 133, 398 and 402 eV in P_{2p} and N_{1s} regions, which were attributed to the phosphorus of the phosphate group, the nitrogen atoms in the urethane or urea bond (-NH-) and the ammonium group ($-N^+(CH_3)_3$), respectively. Then, PC group was clearly observed on the SPUPC-2c film surface. However, these peaks were not so clear on the surfaces of SPUPC-2a and 2b films. Therefore, in this poly(urethane-urea) system, PC content should be over *ca.* 25 wt.% to make the PC group clearly appear on the surface of polymer film. In addition, it was found from the surface analysis, that the PC group was easily rearranged by the immersion in water. Moreover, such PC-containing poly(urethane-urea), SPUPC series, has the higher biocompatibility than PC-containing polyamide, CPAPC series, which would be due to the additive effect of PC unit to the potential biocompatibility of segmented polyurethane.

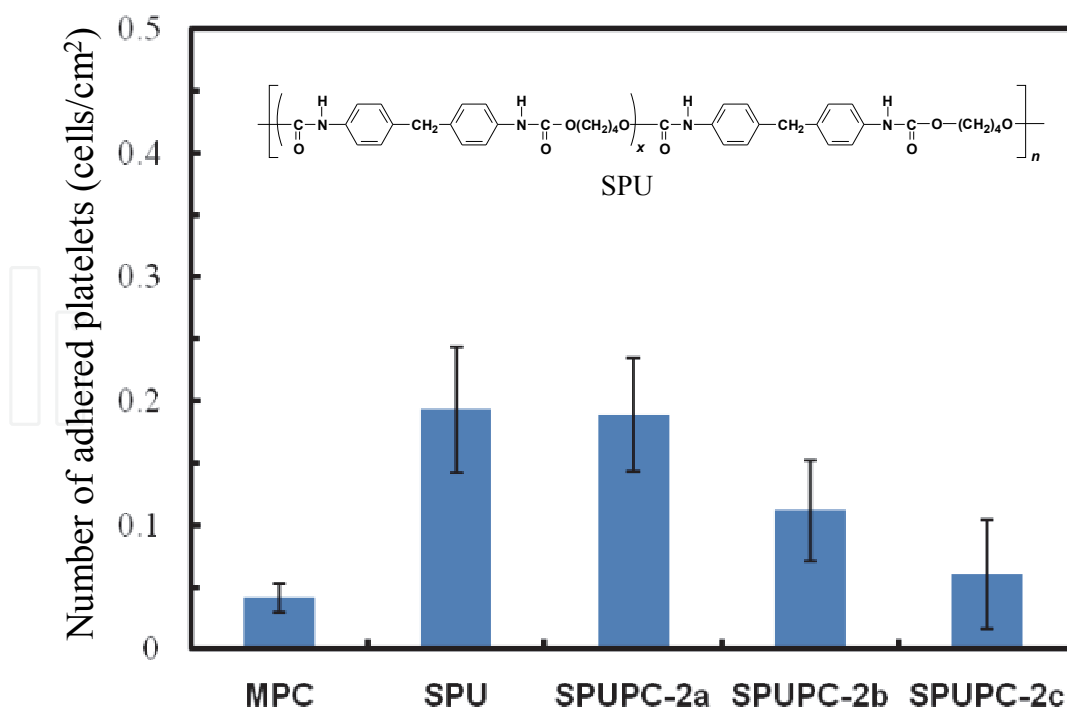


Fig. 5. Amount of adhered platelets on segmented polyurethane, poly(urethane-urea) and MPC polymer films after contact with human PRP for 1 h.

4.3 Mechanical property

From the results of DSC and TGA measurements, PC-containing poly(urethane-urea)s were glassy polymers, T_g of which was not observed in the range of -50°C - 250°C , and the thermal degradation temperature was confirmed at around 250°C . This is a similar thermal behavior as PC-containing polyamides. The characteristic property of such a polyurethane material is a mechanical strength and elasticity. Then, the stress-strain behaviors of PC-containing poly(urethane-urea) films were evaluated in order to reveal the effect of introduction of PC unit on the mechanical property of polyurethane backbone.

Fig. 6 shows the stress-strain behaviors of SPUPC-2a, 2b and 2c films, and the Young's modulus, the tensile strength and the elongation to break were summarized in the table as compared with those of SPU. The similar tendency of stress-strain curve was observed in SPU film, although the Young's moduli and elongations were different. Therefore, there was almost no change in such elastic stress-strain behaviors between SPU and SPUPC series. Young's moduli of SPUPC series increased with the increase of PC unit, as listed in the table of Fig. 6. It would be due to the increase of urea bond, which would enhance the molecular interaction in the hard segments rather than urethane bond. Consequently, the physical properties of these poly(urethane-urea)s obviously depended on the elastic segmented polyurethane backbone.

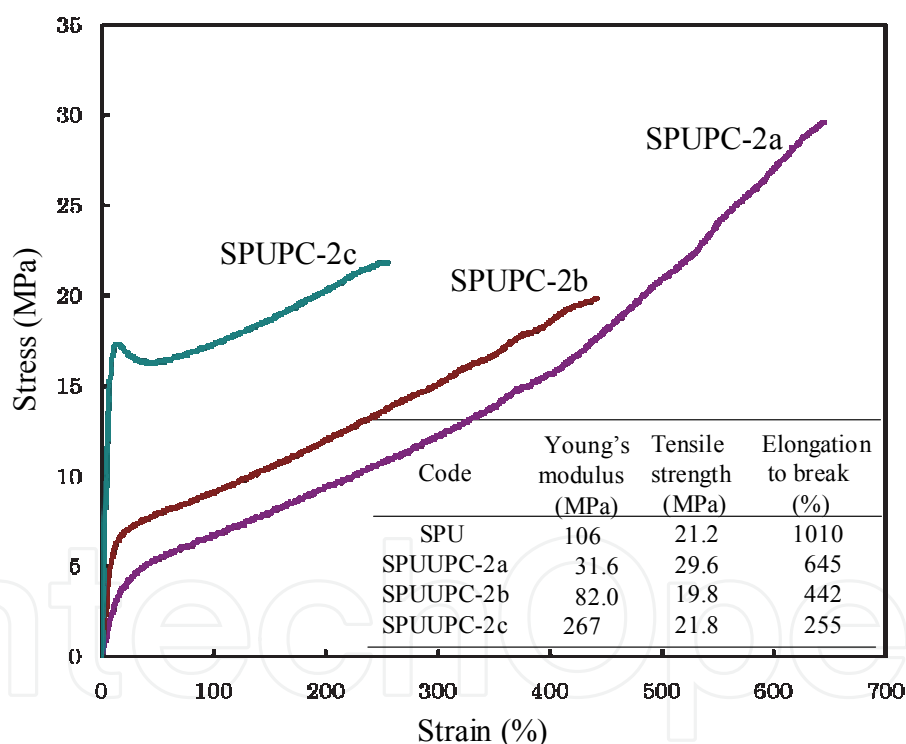


Fig. 6. Stress-strain behaviors of SPUPC films.

Taking such mechanical property into account, we have attempted to prepare the elastic tube from these polyurethane materials. A stainless steel stick ($4\text{ mm}\phi$) was dipped in 5 wt.% SPUPC-2c solution in NMP and dried at 70°C . This procedure was repeated six times, and the copolymer was coated on the stainless steel stick. Then, the coated stick was coated again with poly(carbonate urethane) (Bionate[®] 80A, Asahi Chemical Co.) by the same procedure. After dried, the stainless steel was pulled out carefully to obtain the flexible tube consisted of the composite polyurethanes. The picture of the obtained tube is shown in Fig.

7(a). Fig. 7(b) represents a cross section of the tube by the observation of SEM. In addition, the both side surfaces of the tube were analyzed by XPS, as shown in Fig. 7(c). The phosphorus of PC group was clearly observed inside of the tube at 133 eV, and the outside was confirmed to be coated by poly(carbonate urethane) without PC unit. Therefore, SPUPC-2c/poly(carbonate urethane) composite tube could be successfully prepared.

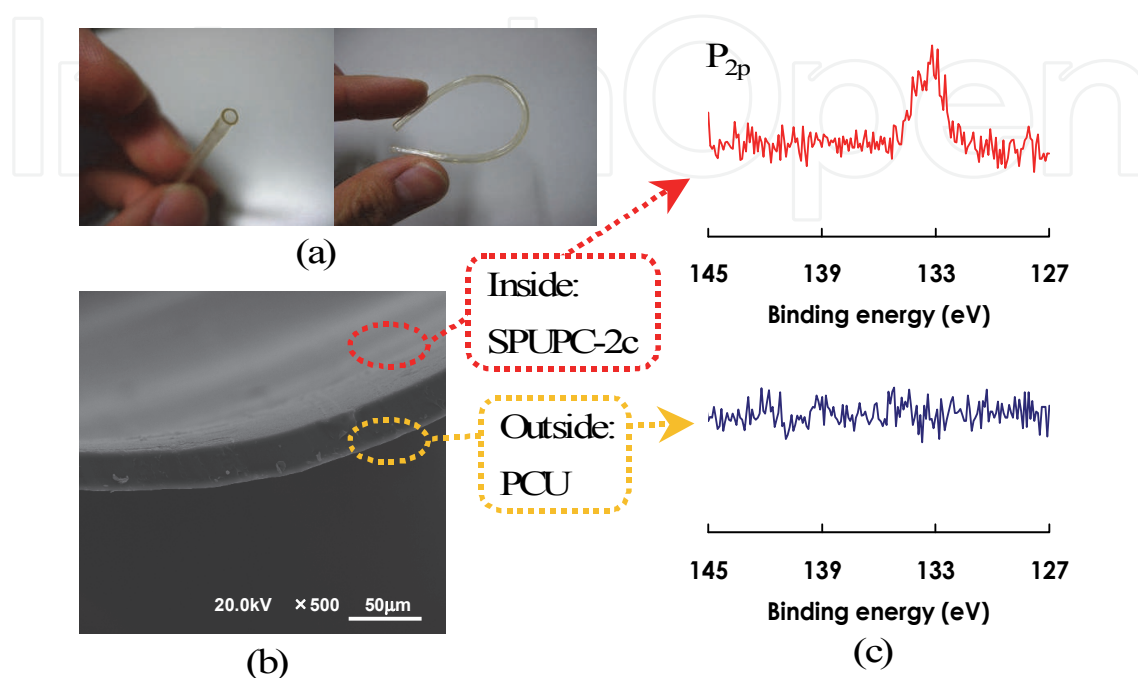


Fig. 7. Polyurethane composite tube made from SPUPC-2c and poly(carbonate urethane) (PCU). (a) Pictures of the tube. (b) SEM picture of the cross section of the tube. (c) XPS spectra of inside and outside of the tube.

The obtained tube has an elastic property derived from segmented polyurethane, and it is expected as artificial blood tube or catheter. The evaluations of this material for implant applications will be carried out in the future, although biomedical researchers are necessary as co-workers for the experiments.

5. Conclusion

This chapter covered the subject of our recent study to develop new biomaterials containing a phospholipid moiety. A novel aromatic diamine monomer containing PC group could be synthesized to prepare polycondensation or polyaddition type polymers. The PC-containing aromatic copolyamides and segmented poly(urethane-urea)s were successfully prepared from the monomer compound. Regarding the effect of PC group on the blood compatibility, the introduction of such a polar group of phospholipid was effective to appear the blood compatibility even in the aromatic copolyamides and segmented poly(urethane-urea)s. It is expected that these copolymers containing PC group will be useful polymeric biomaterials to develop a new generation of biomedical devices, because of the different solubility, the higher thermal stability and the similar biocompatibility as compared to MPC polymer. In addition, aromatic polyamides are hard materials, while segmented poly(urethane-urea)s are soft and elastic materials owing to the nature of main chain components. Therefore, we

can add the several mechanical properties on PC-containing polymers according to any demands of medical applications. For example, the hard material is useful for artificial bone or joint, and the soft and elastic material will be used for artificial blood tube or catheter. It has been also revealed that the biocompatibility is improved satisfactorily as the increase of PC content in the copolymer. However, in the case of these polycondensation or polyaddition type polymers, it is a problem that the solubility in organic solvents becomes poor as the PC content increases. It would be due to the high molecular interaction between side chain PC group and polar group in main chain, such as amide or urea bond. Furthermore, in the case of poly(urethane-urea) system, the increase of urea unit containing PC moiety let the polymer lose the elasticity owing to the aggregation between urea bonds. To solve these problems, we have designed a new diol monomer containing PC moiety, which will be able to yield PC-containing polyurethanes or polyesters. By using the diol monomer, polyurethanes or polyesters with high content of PC unit will be developed, which is now in progress.

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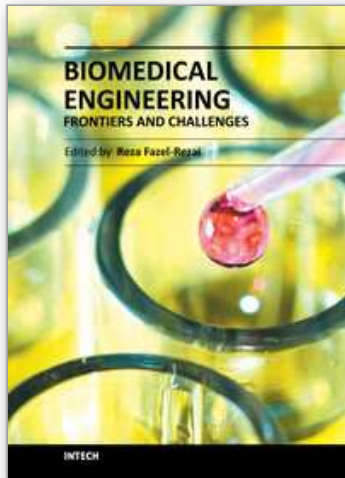
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