DOI: 10.1002/masy.201100034

The Influence of Zwitterionic Phospholipid Brushes Grafted via UV-Initiated or SI-ATR Polymerization on the Hemocompatibility of Polycarbonateurethane

Yakai Feng,[1,2] Dazhi Yang,[1] Marc Behl,[2,3] Andreas Lendlein,[2,3] Haiyang Zhao,[1] Jintang Guo*[1,2]*

Summary: Biomimetic phosphorylcholine (PC) groups were introduced onto material surfaces in order to improve the hydrophilicity and in this way the hemocompatibility of polycarbonateurethanes (PCUs). Surface-initiated atom transfer radical polymerization (SI-ATRP) of 2-methacryloyloxyethyl phosphorylcholine (MPC) initiated by irradiation with ultraviolet (UV) light created polymer brushes having PC side groups. Fourier transform infrared (FTIR), X-ray photoelectron spectroscopy (XPS), scanning electrical microscopy (SEM) and water contact angle were used to characterize the chemical and physical properties of the modified PCU surfaces. The PC-grafted PCU surfaces showed a significantly higher hydrophilicity as indicated by low water contact angles when compared with original PCU. The *in vitro* hemocompatibility of the PC-grafted PCU surfaces was evaluated by platelet adhesion tests. The PCU surfaces modified with phosphorylcholine zwitterionic brushes showed effective resistance for platelet adhesion and high hemocompatibility. These PC-grafted PCU materials might be potentially applied in blood-contacting materials or devices due to their good mechanical and hemocompatible properties.

Keywords: ATRP; hemocompatibility; phosphorylcholine; polycarbonateurethane; surface modification; UV grafting

Introduction

Polycarbonateurethanes (PCUs) are being investigated as materials for medical devices due to their versatile mechanical properties and their relatively beneficial hemocompatibility.[1–7] Nevertheless, thrombus formation can still occur when artificial organs and biomedical devices made of PCUs are in contact with blood for an extended period of time.[8–10] Therefore, improving the hemocompatibility of PCUs for biomedical applications is still a significant scientific challenge.

The biomimetic phosphorylcholine (PC)-modified polymers provide resistance to protein adsorption and cell adhesion. They have usually been used to modify the surface of blood-contacting materials and implantable medical devices.[11–14] The zwitterionic phospholipid group is found in cell membranes and possesses nonthrombogenic properties and high biocompatibility. The PC groups of modified surfaces could tightly bind water molecules on the topmost part of the surface and form a uniform water layer on the surface. This bound water layer could efficiently reduce the interaction between material surface and protein, which plays a dominant role in the resistance to nonspecific protein adsorption on material surface.[15,16]

---

[1] School of Chemical Engineering and Technology, Tianjin University, Tianjin 300072, China
E-mail: jintang_guo@hotmail.com, yakaifeng@hotmail.com

[2] Tianjin University-Helmholtz-Zentrum Geesthacht, Joint Laboratory for Biomaterials and Regenerative Medicine, Weijin Road 92, 300072 Tianjin, China, Kantstr. 55, 14513 Teltow, Germany

[3] Center for Biomaterial Development and Berlin Brandenburg Center for Regenerative Therapies (BCRT), Institute of Polymer Research, Helmholtz-Zentrum Geesthacht, Kantstr. 55, 14513 Teltow, Germany

UV-photografting polymerization is a promising method for the surface modification of polymers because it is a relatively simple, energy-efficient, and cost-effective process.[17-19] Recently, we have investigated the surface modification of PCU by grafting polymerization of hydrophilic poly(ethylene glycol) monoacrylate (PEGMA) macromonomer.[20] The grafting density increased with the increase of PEGMA and initiator concentration, whereas reaction temperature showed slight influence on the grafting density. Prolonging UV irradiation time was favorable to the grafting density, but when irradiation time was above 90 min, the photolysis of grafted chains competed with photopolymerization, resulting in low grafting density. The photografted PCU surfaces exhibited excellent hydrophilicity owing to the hydrophilic poly(PEGMA) blocks on the surface.

The UV polymerization could result in high grafting density, but the molecular weight of the grafting chains was difficult to be controlled. In our previous research, the surface of PCU was modified by UV grafting polymerization of PEGMA macromonomer. In the process of UV polymerization, the initiator can cleave a hydrogen atom from the polymer main chains, resulting in side reactions and a uncontrollable surface structure, although there is a low probability of occurrence. Here we explored whether surface-initiated atom transfer radical polymerization (SI-ATRP) can be used to introduce controllable grafting chains onto the PCU surface.

SI-ATRP is particularly practical for preparing well-defined surface because of its versatility with respect to the type of monomers, its tolerance of impurities, and typically mild reaction conditions under which it is conducted.[21] The length of grafting chains can be easily controlled by SI-ATRP, so the adequate length of grafting chains is designed on the PCU surface to meet the need of convenient application. With its living character, the ATRP process yields polymers with a low polydispersity and permits the synthesis of block copolymers by the activation of dormant chain ends.[22,23]

As expected, the hemocompatibility of PCU surface could be improved via grafting 2-methacryloyloxyethyl phosphorylcholine (MPC). MPC has been widely used to construct non-biofouling surfaces in various biomedical applications because PC group has been found to resist both protein adsorption and cell adhesion.[24,25]

In this study, we attempted to prepare highly hydrophilic and hemocompatible PCU surface containing phosphorylcholine groups via grafting MPC by UV photo-induced polymerization and by SI-ATRP (Scheme 1). The zwitterionic brush structure was constructed on the PCU surface in order to increase phosphorylcholine content. The grafting results by these two surface modification methods were discussed. The biocompatibility of the modified PCU films was also evaluated.

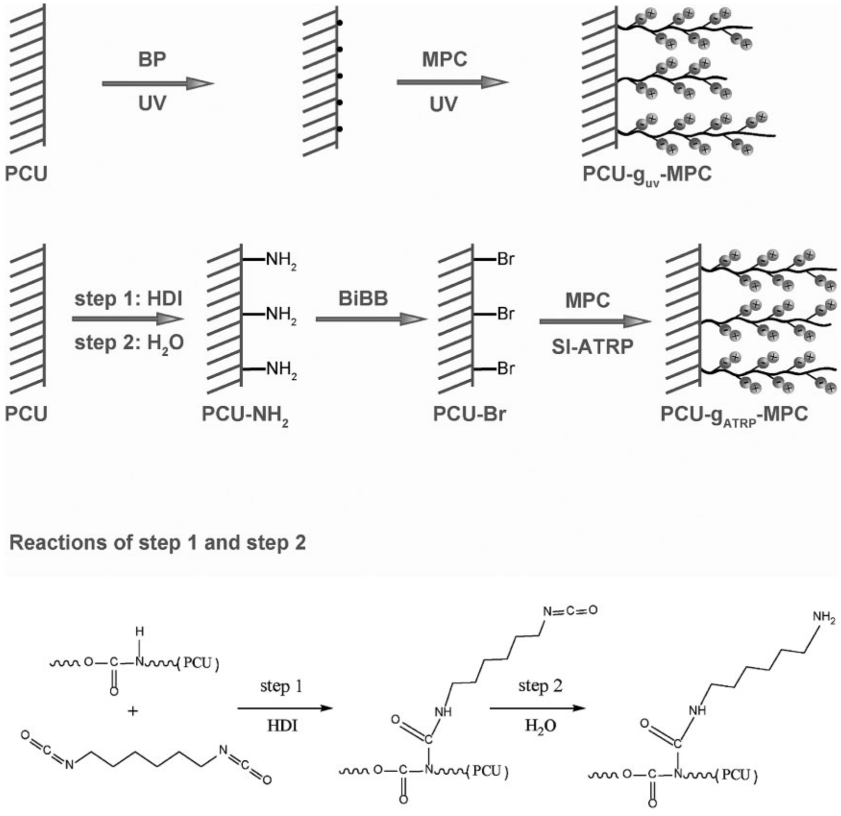
Experimental Part

Materials

Polycarbonateurethane (PCU, Chronoflex C) with a number average molecular weight of $1.1 \times 10^5\,g \cdot mol^{-1}$ was purchased from Cardio International Incorporated, USA. Benzophenone (99+ %, BP) as a photo-initiator was purchased from Tianjin Jiangtian Chemical Technology Company Ltd, China. MPC was purchased from Nanjing Joy Nature Technology Institute, China. 2-Bromoisobutyryl bromide (BiBB), 2,2′-bipyridine (Bipy), CuBr and $CuBr_2$ were purchased from Sigma-Aldrich Co, Shanghai, China. All other chemicals were analytical grade and were commercially available.

Preparation of PCU Films

A suitable amount of PCU was dissolved in THF to prepare 8 wt% solution. The solution was evenly spread on a glass petri dish, which was aligned perfectly horizontal to ensure that film had uniform thickness. The dish was kept in a chemical hood for 48 h to allow the THF to evaporate. The



Scheme 1.
Schematic illustration of grafting phosphorylcholine brushes on PCU surface by UV polymerization and SI-ATRP.

film was removed from the petri dish and cleaned in ethanol by ultrasonic cleaner for 10 min, finally the film was completely dried at 60 °C for 12 h under high vacuum. The prepared film was cut into $2.5 \times 4.0\,\text{cm}^2$ pieces as specimen for surface modification experiments.

Preparation of PCU–g$_{UV}$-MPC by UV Grafting Polymerization

The pre-weighted PCU films (w_0) were dipped into an acetone solution containing BP ($100\,\text{mg}\cdot\text{mL}^{-1}$) as a photoinitiator, removed from the solution and then dried in air for 30 min in the dark to obtain PCU films containing BP on the surface. The dried films were clamped with self-made fixtures, subsequently immersed into 2.5 wt% MPC aqueous solution, and then placed in the ultraviolet reactor. After purging with nitrogen gas for 10 min, MPC was photografted onto the PCU films at 60 °C for 60 min under UV irradiation with a 300 W high pressure mercury lamp while the inert conditions were maintained. The distance between the PCU film and the UV lamp was set 18 cm. After irradiation, the grafted films were removed from the reactor and washed with ethanol by ultrasound shaking water bath to remove absorbed oligomer, homopolymers and unreacted monomer for 8 h, and then further washed with pure water for 24 h. After dried in a vacuum oven at 60 °C to constant weight, the films were weighed to obtain the weight of the PC-grafted films (w_1).

Preparation of PCU-NH$_2$ Film

Firstly, hexamethylene diisocyanate (HDI) was grafted onto the PCU surface to obtain

PCU-HDI film through the allophanate reaction between urethane proton and the isocyanate group of HDI in the presence of dibutyltin dilaurate (DBTDL). PCU-HDI film was prepared according to the method described by Tan and Obendorf[26] and Yuan et al.[27]

Dry toluene (40 mL), HDI (4.0 g) and DBTDL (0.040 g) were introduced in a flask. The PCU film (2.0×2.0 cm^2) was totally immersed into the reactive solution at 50 °C for 1.5 h, and then the film was washed with n-hexane in an ultrasonic cleaner for 10 min to remove the unreacted HDI. The PCU-HDI film was immersed into water at 50 °C for 24 h. The PCU-NH_2 film was obtained and washed with pure water three times and dried in a vacuum oven at 60 °C until constant weight.

Preparation of PCU-Br Film

In a 150 mL three-necked round-bottom flask, 50 mL toluene and 0.5 mL triethylamine (TEA) were mixed and the PCU-NH_2 film was immersed in this solution, subsequently 1.0 mL BiBB in 10 mL toluene was slowly dropped into the flask at 0 °C, cooled by an ice/water bath. The reaction mixture was further stirred at room temperature overnight. The obtained PCU-Br film was removed, washed with toluene and pure water, and then dried at 50 °C in vacuum overnight.

Preparation of PCU–g$_{ATRP}$-MPC by SI-ATRP Method

Argon gas was purged in methanol and water to eliminate oxygen before polymerization. The molar ratio of catalyst compositions was as follows: [CuBr]:[Bipy]:[$CuBr_2$] = 1:2:1. MPC (0.01 mol), $CuBr_2$ and Bipy were added to the Schlenk flask containing a magnetic stirring bar and subsequently dissolved in 10 mL methanol and 30 mL pure water bubbled with argon to eliminate oxygen. After stirring for 30 min, the PCU-Br film was submerged to the flask. CuBr was added and formed the complex CuBr-Bipy acting as ATRP-catalyst. The graft polymerization was performed at 50 °C with stirring for 24 h under an argon gas atmosphere. After reaction, the PCU-g$_{ATRP}$-MPC film was extracted with methanol for 24 h to remove the unreacted reagents and homopolymers. Subsequently, the film was dried in vacuum at room temperature until constant weight.

Characterization

Transmission Fourier transform infrared (FTIR) spectra of surfaces were characterized by Bio-Rad FTS-6000 in transmission mode by Fourier transform infrared spectrometer. Chemical elements and their status of the films were determined by PHI-1600 X-ray photoelectron spectroscopy (XPS) with a Mg Kα X-ray source under 2×10^{-8} Torr. The core-level signals were obtained at a photoelectron take-off angle of 45°. The elemental compositions were calculated from peak areas, and spectra bands of C1s were deconvoluted into sub-peaks by the XPSPEAK41 spectrometer software. Surface morphologies of the films were observed with Nova NanoSEM 430 scanning electrical microscopy (SEM).

Grafting Density and Water Uptake

The grafting density (GD) of MPC on PCUs was calculated by the following formula:

$$\mathrm{GD}\,(\mathrm{mg} \cdot \mathrm{cm}^{-2}) = (w_1 - w_0)/S$$

where w_0 and w_1 were the weight of the blank film and the PC-modified film, respectively, and S was the surface area of the PCU film. The average GD was calculated by three parallel experiments.

Hygroscopicity was measured by soaking the modified films in distilled water at room temperature for 24 h, removing from the water bath and wiping rapidly with filter paper, and then weighing them immediately (w_2). The water content of the films was calculated as the ratio of the absorbed water to dried film weight. The hygroscopicity of grafted films was characterized by water uptake per unit area (WU) according to the formula:

$$\mathrm{WU}\,(\mathrm{mgcm}^{-2}) = (w_2 - w_1)/S$$

where w_2 was the weight of the modified film after absorbed water for 24 h. WU values were given as the average of three parallel experiments.

Water Contact Angle Measurement

Wettability of the MPC grafted PCU surface was characterized by static contact angle measurement using the sessile drop technique. The measurements were performed at room temperature on a Kruss EasyDrop goniometer (Kruess GmbH, Germany) equipped with a digital photoanalyzer using 3 μL distilled water. The values of the contact angles were calculated as the average of six measurements.

Platelet Adhesion Test

Ethics Statement

All animals were handled in strict accordance with good animal practice as defined by the relevant local animal welfare bodies, and all animal work was approved by the Animal Research Committee of the Tianjin University.

Fresh rabbit blood was centrifuged at 2000 rpm for about 15 min to prepare platelet-rich plasma (PRP) for the platelet adhesion experiment. The films were placed in a 24-well tissue culture plate and immersed in phosphate buffered saline (PBS, pH 7.4) for 12 h. Subsequently, the PRP was dropped into new wells and the films were incubated at 37 °C for 4 h. After rinsing with PBS three times to remove any non-adhered platelets, the films were transferred into new wells and fixed for 30 min in 2.5% glutaraldehyde in PBS, dehydrated by a series of graded alcohol-water solutions (50, 60, 70, 80, 90 and 100%) for 30 min in each step, and dried under vacuum. After that, the films were coated with gold for examination in Nova NanoSEM 430 scanning electrical microscopy (SEM). Four different regions were observed on each film.

Hemolytic Rate

The hemolytic rate was calculated according to the following formula:

$$\text{Hemolytic Rate}\,\% = \frac{\mathrm{A} - \mathrm{B}}{\mathrm{C} - \mathrm{B}} \times 100\%$$

where A is the optical density (OD) at 545 nm of the solution with test materials, B the OD of negative control, and C the OD of positive control.

Results and Discussion

FTIR Spectra of PCU and Modified PCU Films

Scheme 1 shows the schematic processes of grafting phosphorylcholine brushes on the PCU surface by UV polymerization and SI-ATRP. PCU-g_{UV}-MPC films were modified films by UV polymerization at 60 °C for 60 min, whereas PCU-g_{ATRP}-MPC films were prepared by SI-ATRP. For SI-ATRP, firstly, the NCO groups were introduced onto PCU film by the reaction of urethane groups with HDI, and then PCU-NH_2 film was prepared by the hydrolysis of isocyanate of PCU-NCO with water. Catalyzed by TEA, BiBB reacted easily with the amino groups of the PCU-NH_2 film to introduce tertiary bromine on the surface, which acted as the initiator for SI-ATRP. Finally, PCU-g_{ATRP}-MPC films were prepared by grafting MPC via SI-ATRP (Scheme 1).

The PCU films were characterized by FTIR spectroscopy before and after construction of zwitterionic phosphorylcholine brushes onto PCU surface. Figure 1 shows the FTIR spectrum of the blank PCU film.

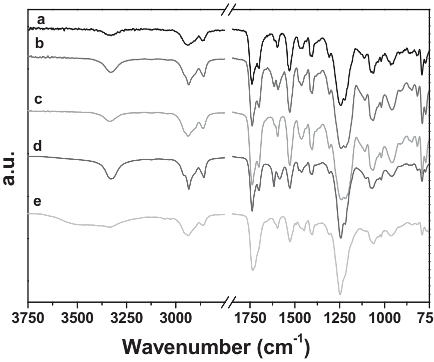


Figure 1.
FTIR spectra of PCU film (a); PCU-NH_2 film (b); PCU-Br film (c); PCU-g_{ATRP}-DMAPS film (d); PCU-g_{UV}-MPC film (e).

The peaks at 2939 cm^{-1} and 2863 cm^{-1} correspond to the anti-symmetric and symmetrical stretch vibration peaks of CH_2 in PCU. The absorption peaks at 1724 cm^{-1} and 1530 cm^{-1} can be assigned to the carbonyl group and the C-N bond, respectively. The peak at 1466 cm^{-1} was the symmetry bending vibration peak of the CH_2. The 1253 cm^{-1} peak was assigned to C–O–C stretching in the polycarbonate segments.

Both grafted films, the PCU-g_{ATRP}-MPC and the PCU-g_{UV}-MPC display sharp peaks at 1250 cm^{-1}, which can be ascribed to the overlap between P=O in the MPC moiety[28] and C–O–C stretching in the polycarbonate segments. The absorption peaks of $N^+(CH_3)_3$ and C–O–P at 970 cm^{-1} and 800 cm^{-1} were overlapped by the peaks of PCU in the finger print region.

XPS Spectroscopy of PCU and Modified PCU Films

The XPS spectra of blank PCU surface and modified PCU surfaces illustrated the changes of C, N, O, P and Br compositions on the surface layer before and after grafting MPC. Elemental compositions of the blank PCU and the surface-modified PCU were calculated from XPS results and listed in Table 1. From the Table 1, Br(3d) content was 0.5% on the PCU-Br film, which proved the successful introduction of bromine on the tertiary carbon on the surface, which could act as the initiator for SI-ATRP. The P(2p) content on the PCU-g_{ATRP}-MPC film and PCU-g_{UV}-MPC film was 0.8% and 3.2%, respectively, while P(2p) peak was not observed on the blank PCU film. The P(2p) content determined in the PCU-g_{UV}-MPC film was significantly higher compared to the PCU-g_{ATRP}-MPC film.

Table 1.
Elemental compositions of the PCU film and modified PCU films by XPS.

Sample ID	Atomic content (%)				
	C (1s)	O (1s)	N (1s)	P (2p)	Br (3d)
PCU film	77.9	20.3	1.9	0.0	0.0
PCU-NH_2 film	74.8	22.0	3.2	0.0	0.0
PCU-Br film	71.7	23.2	4.6	0.0	0.5
PCU-g_{ATRP}-MPC film	69.3	26.7	3.2	0.8	0.0
PCU-g_{UV}-MPC film	70.3	23.4	3.1	3.2	0.0

From Figure 2, the P(2p) peak was observed in the MPC grafted PCU films compared with the blank PCU film (Figure 3). This change in P(2p) intensity was also found in other experimental conditions when MPC was grafted onto PCU films via UV polymerization and SI-ATRP method. The XPS results indicated a successful grafting of MPC onto the PCU surface by both grafting polymerization methods.

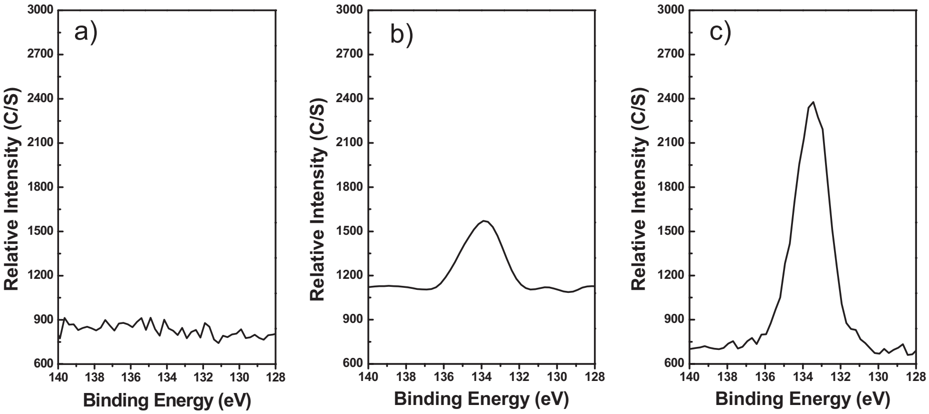


Figure 2.
P(2p) XPS spectra of PCU film (a), PCU-g_{ATRP}-MPC film (b) and PCU-g_{UV}-MPC film (c).

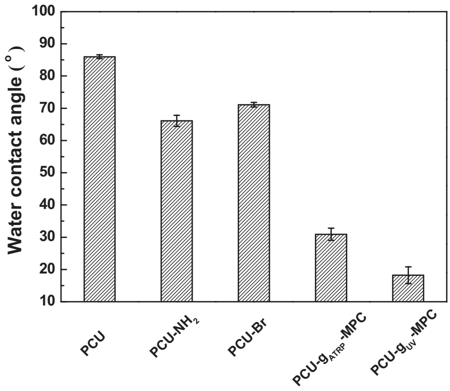


Figure 3.
Water contact angles of PCU film, PCU-NH_2 film, PCU-Br film, PCU-g_{ATRP}-MPC film and PCU-g_{UV}-MPC film.

Influence of UV Polymerization and SI-ATRP on Grafting Effect

MPC was grafted on PCU surface by UV polymerization and SI-ATRP. The grafting density of MPC on the PCU film varied significantly by these two methods. In UV grafting polymerization, the grafting density of the PCU-g_{uv}-MPC film was found to be $0.5\,mg \cdot cm^{-2}$, while the PCU-g_{ATRP}-MPC film obtained by SI-ATRP modified method showed lower grafting density ($0.1\,mg \cdot cm^{-2}$). As expected, UV polymerization was influenced mainly by the initiator concentration when other polymerization conditions were not changed. In SI-ATRP the grafting density was low because of the low bromine on tertiary-carbon as initiator. By optimizing the reaction conditions, the PCU-Br with high bromine content could be obtained.

Water Contact Angle of PCU and Modified PCU Films

Water contact angle measurements were used to characterize interfacial hydrophilic properties. The phosphorylcholine groups and polymethacrylate chains on PCU-g-MPC surfaces were favorable for improving surface hydrophilicity. The phosphorylcholine groups were more hydrophilic than the polymethacrylate chains, which resulted in low water contact angle value of both PCU-g-MPC surfaces. Before grafting modification, the PCU film exhibited hydrophobic properties with a high water contact angle (86.0°), the hydrophilicity of PCU-NH_2 increased (66.1°) resulting from the introduction of amine groups onto the PCU surface, while water contact angle of PCU-Br was 71.1°. PCU film modified with MPC showed hydrophilic properties as indicated by low water contact angle (Figure 3). The results confirmed that two effective modification methods of the PCU surface were successfully carried out by two grafting polymerization processes. The film modified by UV polymerization showed lower water contact angle (18.2°) than the film modified by SI-ATRP (30.9°) because of the higher grafting density of UV modified film.

Water Uptake of PCU and Modified PCU Films

The amount of adsorbed water was measured to estimate the hydrophilicity of the grafted layers formed on the PCU films. The water uptake per-unit area of modified PCU film was influenced by the hydrophilicity of surface, grafting density, and the structures of grafted layer. Therefore, the results of water uptake reflected the hydrophilicity of grafted films.

The modified PCU films were soaked in distilled water for 24 h at 25 °C to ensure equilibrium adsorption. It was well known that the water uptake of the hydrophobic blank PCU film is very low, which was confirmed in a determined value only $0.28\,mg \cdot cm^{-2}$. The water uptake of PCU-NH_2 and PCU-Br was $0.55\,mg \cdot cm^{-2}$ and $0.63\,mg \cdot cm^{-2}$, respectively, and slightly higher than the value obtained for blank PCU, due to the high hydrophilic property compared with blank PCU. Whereas the water uptake of the MPC grafted PCU films significantly increased up to 1.33 and $1.62\,mg \cdot cm^{-2}$ for PCU-g_{ATRP}-MPC film and PCU-g_{UV}-MPC film, respectively (Figure 4). Zwitterions provide a strong hydration layer via electrostatic interaction. When the surface of modified material has a

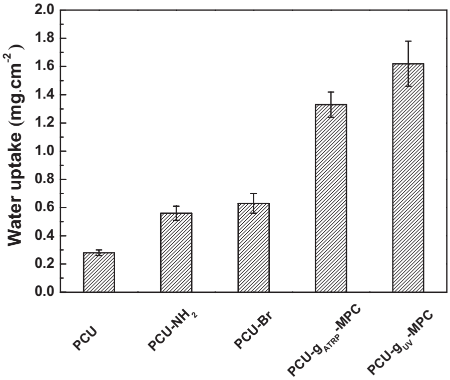


Figure 4.
Water uptake of PCU film, PCU-NH$_2$ film, PCU-Br film, PCU-g$_{ATRP}$-MPC film and PCU-g$_{UV}$-MPC film.

certain amount of zwitterions grafted, the adsorption of water can reach only an equilibrium.[15] When the extent of grafting was increased, no additional water can be adsorbed onto the material surface. Therefore, the water uptake of PCU-g$_{ATRP}$-MPC film and PCU-g$_{UV}$-MPC film showed little difference.

Platelet Adhesion and Haemolysis Studies of PCU and Modified PCU Films

The hemocompatibility of the MPC grafted films was evaluated by platelet adhesion in PRP using the PCU film as the reference. After the initiator Br was immobilized on the PCU surface, a substantial number of platelets adhered and aggregated with extended pseudopodia (Figure 5b). This may be because protein adsorption on hydrophobic surface was higher resulting in a higher activation and adhesion of platelets. From SEM photographs (Figure 5c and Figure 5d), nearly no platelets were observed for the MPC grafted films when incubated for 4 h, while the PCU film was covered with a large number platelets. Phosphorylcholine

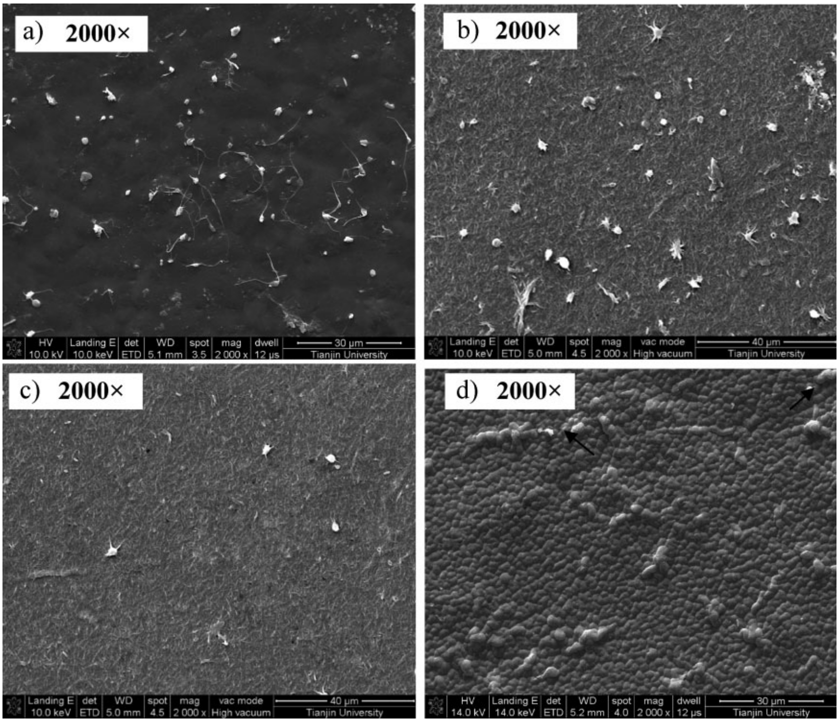


Figure 5.
SEM photographs of platelet adhesion tests *in vitro* after incubation 4 h in PRP: PCU film (a), PCU-Br film (b), PCU-g$_{ATRP}$-MPC film (c), and PCU-g$_{UV}$-MPC film (d).

groups of MPC grafted PCU film surface could tightly bind water molecules on the topmost part of the surface and form uniform water layer on the film surface. This bound water layer could efficiently reduce the interaction between proteins and film surface, which played a dominant role in the surface resistance of nonspecific protein adsorption. The hemolytic rates of PCU and modified PCU films were less than 5%, which is the requirement of blood-contacting materials for medical applications. Meanwhile, the hemolytic rate of the MPC modified PCU film (0.3) was less than that of PCU film (1.4). Based on above results, zwitterionic phosphorylcholine brush structure could efficiently prevent platelet adhesion and improve the blood compatibility.

Conclusion

Biomimetic, zwitterionic PC groups could be successfully introduced onto PCU surface via UV irradiation polymerization as well as by SI-ATRP. The modified PCU surfaces obtained by both grafting methods exhibited excellent hydrophilicity owing to the brush structure of zwitterionic PC groups. Higher grafting density could be achieved by UV polymerization compared to grafting by the SI-ATRP method. Nearly no platelets were adsorbed on the modified film surfaces. The PCU surfaces modified with zwitterionic phosphorylcholine brushes showed effective resistance to platelet adhesion and high hemocompatibility *in vitro*. These PC-grafted PCU materials might be potentially applied in blood-contacting materials or devices due to their good mechanical and hemocompatible properties.[29]

Acknowledgements: This work has been supported by the Program for New Century Excellent Talents in University NCET-07-0596, Ministry of Education of P. R. China, the International Cooperation from Ministry of Science and Technology of China (Grant No. 2008DFA51170) as well as by the Tianjin University-Helmholtz-Zentrum Geesthacht Joint Laboratory for Biomaterials and Regenerative Medicine, which is financed by MOST and the German Federal Ministry of Education and Research (BMBF) (Grant No. 0314596).

[1] H. Y. Zhao, Y. K. Feng, J. T. Guo, *J. Appl. Polym. Sci.* **2011**, in press

[2] J. Guo, Y. Feng, Y. Ye, H. Zhao, *J. Appl. Polym. Sci.* **2011**, in press

[3] S. Zhang, Y. Feng, L. Zhang, J. Guo, Y. Xu, *J. Appl. Polym. Sci.* **2010**, *116*, 861.

[4] M. Behl, J. Zotzmann, A. Lendlein, *Adv. Polym. Sci.* **2010**, *226*, 1.

[5] A. Lendlein, M. Behl, B. Hiebl, C. Wischke, *Expert. Rev. Med. Devic.* **2010**, *7*(3), 357.

[6] J. T. Guo, Y. Q. Ye, Y. K. Feng, H. Y. Zhao, *Polym. Adv. Technol.* **2010**, *21*, 759.

[7] L. Xue, H. P. Greisler, *J. Vasc. Surg.* **2003**, *37*, 472.

[8] K. Y. Chen, J. F. Kuo, C. Y. Chen, *Biomaterials* **2000**, *21*, 161.

[9] P. A. Gunatillake, D. J. Martin, G. F. Meijs, S. J. McCarthy, R. Adhikari, *Aust. J. Chem.* **2003**, *56*, 545.

[10] P. D'Arrigo, C. Giordano, P. Macchi, L. Malpezzi, G. Pedrocchi-Fantoni, S. Servi, *Int. J. Artif. Organs.* **2007**, *30*, 133.

[11] K. Ishihara, D. Nishiuchi, J. Watanabe, Y. Iwasaki, *Biomaterials* **2004**, *25*, 1115.

[12] N. Morimoto, A. Watanabe, Y. Iwasaki, K. Akiyoshi, K. Ishihara, *Biomaterials* **2004**, *25*, 5353.

[13] T. Goda, R. Matsuno, T. Konno, M. Takai, K. Ishihara, *Colloid Surface B* **2008**, *63*, 64.

[14] T. Goda, R. Matsuno, T. Konno, M. Takai, K. Ishihara, *J. Biomed. Mater. Res. B* **2009**, *89B*, 184.

[15] S. F. Chen, J. Zheng, L. Y. Li, S. Y. Jiang, *J. Am. Chem. Soc.* **2005**, *127*, 14473.

[16] S. F. Chen, F. C. Yu, Q. M. Yu, Y. He, S. Y. Jiang, *Langmuir.* **2006**, *22*, 8186.

[17] A. Bhattacharya, B. N. Misra, *Prog. Polym. Sci.* **2004**, *29*, 767.

[18] D. He, H. Susanto, M. Ulbricht, *Prog. Polym. Sci.* **2009**, *34*, 62.

[19] Y. K. Feng, H. Y. Zhao, L. Zhang, J. T. Guo, *Front. Chem. Eng. Chin.* **2010**, *4*, 372.

[20] H. Y. Zhao, Y. K. Feng, J. T. Guo, *J. Appl. Polym. Sci.* **2011**, *119*, 3717.

[21] J. B. Kim, W. X. Huang, M. D. Miller, G. L. Baker, M. L. Bruening, *J. Polym. Sci. Poly. Chem.* **2003**, *41*, 386.

[22] S. Edmondson, V. L. Osborne, W. T. S. Huck, *Chem. Soc. Rev.* **2004**, *33*, 14.

[23] Y. Iwasaki, K. Ishihara, *Anal. Bioanal. Chem.* **2005**, *381*, 534.

[24] M. Kyomoto, T. Moro, Y. Takatori, H. Kawaguchi, K. Nakamura, K. Ishihara, *Biomaterials* **2010**, *31*, 1017.

[25] J. Zhao, Q. A. Shi, L. G. Yin, S. F. Luan, H. C. Shi, L. J. Song, J. H. Yin, P. Stagnaro, *Appl. Surf. Sci.* **2010**, *256*, 7071.

[26] K. Tan, S. K. Obendorf, *J. Membr. Sci.* **2006**, *274*, 150.

[27] J. Yuan, L. Chen, X. F. Jiang, J. Shen, S. C. Lin, *Colloid Surface B* **2004**, *39*, 87.

[28] K. Ishihara, R. Takayama, N. Nakabayashi, K. Fukumoto, J. Aoki, *Biomaterials* **1992**, *13*, 235.

[29] F. Jung, C. Wischke, A. Lendlein, *Mater. Res. Bull.* **2010**, *35*, 607.