Materials Science and Engineering C 45 (2014) 539–545

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Preparation of poly(cyclooctene)-g-poly(ethylene glycol) (PCOE-g-PEG) graft copolymers with tunable PEG side chains via ROMP and its protein adsorption and platelet adhesion properties

Ying Yang [a], Dean Shi [a,*], Xueli Wang [a], Hengchong Shi [b,*], Tao Jiang [a], Yingkui Yang [a], Shifang Luan [b], Jinghua Yin [b,*], Robert K.Y. Li [c]

[a] Ministry-of-Education Key Laboratory for the Green Preparation and Application of Functional Materials, Faculty of Materials Science and Engineering, Hubei University, Wuhan 430062, PR China
[b] State Key Laboratory of Polymer Physics and Chemistry, Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, Changchun 130022, PR China
[c] Department of Physics and Materials Science, City University of Hong Kong, Tat Chee Avenue, Kowloon, Hong Kong, PR China

ARTICLE INFO

Article history:
Received 18 December 2013
Received in revised form 19 August 2014
Accepted 2 October 2014
Available online 5 October 2014

Keywords:
ROMP
Poly(cyclooctene)-g-PEG
Tunable
Protein adsorption
Platelet adhesion

ABSTRACT

In our previous work [H. Shi, D. Shi et al., Polymer Chemistry 2(2011)679–684], polycyclooctene-g-PEG (PCOE-g-PEG) copolymers were synthesized via ring opening metathesis polymerization (ROMP) from PEG functionalized cyclic olefin macromonomers and cyclooctene. The grafting degree and the grafting site were easily controlled through the "grafting through" approach. The PCOE-g-PEG film surface was imparted excellent anti-protein adsorption properties. In that work, the molecular weight of PEG side chain was fixed at 750 g/mol and the neat PEG content in the copolymer was lower than 50 wt.%. In this work, both the effects of PEG side chain lengths (350 to 1000 g/mol) at a fixed PEG content (50 wt.%) and the neat PEG content (30 wt.% to 70 wt.%) at a fixed PEG molecular weight (750 g/mol) on the anti-protein adsorption and anti-platelet adhesion properties are studied. It is shown that the copolymer with 60 wt.% PEG side chains of 750 g/mol, where both PEG and PCOE form continuous morphology, is optimal to reduce the adsorption of both the bovine serum albumin (BSA) and platelet. When the PEG content reaches 70 wt.%, phase inversion happens. PEG is the continuous phase but PCOE becomes the dispersed phase. The surface roughness of the casting PCOE-g-PEG film increases. In this case, both BSA adsorption and platelet adhesion will slightly increase comparing to the sample with 60 wt.% PEG.

1. Introduction

When foreign materials are exposed to blood, plasma proteins should be adsorbed to the surface, which is followed by the platelet adhesion and thrombus formation. Hence, the surfaces with the ability to inhibit proteins adsorption are in desperate need. The surfaces bearing polyethylene oxide coatings have proved in piles of previous studies to be particularly effective in resistance to protein adsorption [1–9]. A lot of approaches were used to prepare the PEG coated membrane for biomaterial applications, such as physical adsorption, plasma deposition, chemical grafting modification and radiation. Amiji prepared PEG modified surfaces via physical adsorption (complexation–interpenetration method) of anionic PEG derivative onto the chitosan surface to improve blood compatibility [10]. Besides, polyethylene glycol acrylate (PEGA) was also adsorbed to hydrophobic substrate surface to enhance protein resistance [11]. However, the defect in PEG surfaces prepared by using simple adsorption techniques is their tendency of yielding elution effect and competitive adsorption [12]. Hence, many other methods were adopted to obtain more stable systems by the covalent immobilization of PEG onto surface. For instance, plasma treatment was used to induce graft-polymerization of polyethylene glycol acrylate (PEGA) on substrate films [11] and elastomer was covalently grafted PEG or PEG derivatives via UV-induced graft polymerization technique [13,14]. All those modified surfaces presented the enhanced anti-protein adsorption ability compared to the virgin surface. However, both plasma and radiation treatment suffered from limitations such as poor grafting efficiency as well as unavoidable side-reactions which resulted in unpredicted surface chemistry. Furthermore, conventional chemical modification methods [15–17] were also often blended with toxic monomer residues in the final products, owing to its high activity and low conversion of monomer. Comparing to the LBL assembly and direct covalent wafer-grafting methods [18–20], directly using graft or block copolymers to fabricate protein-resistant membranes and surfaces receives much attention of researchers in this field because of its simple and convenient method but stable properties. Taking the above problems into consideration, ring opening metathesis polymerization (ROMP) was adopted in our previous work [21]. PCOE-g-PEG copolymers were synthesized via ROMP from PEG functionalized cyclic olefin macromonomers and cyclooctene. The grafting degree and the grafting site were easily

* Corresponding author.
E-mail addresses: deanshi2012@yahoo.com (D. Shi), shihc@ciac.ac.cn (H. Shi), yinjh@ciac.ac.cn (J. Yin).

http://dx.doi.org/10.1016/j.msec.2014.10.010
0928-4931/

controlled through the "grafting through" approach, and the PCOE-g-PEG surface was imparted excellent anti-protein adsorption. However, in that work, only PEG-750 (750 g/mol) was used as the side chain and the effect of PEG chain length on the anti-protein adsorption was not studied. In this work, both the effects of PEG side chain lengths (350 to 1000 g/mol) at a fixed PEG content (50 wt.%) and the neat PEG content (30 wt.% to 70 wt.%) at a fixed PEG molecular weight (750 g/mol) on the anti-protein adsorption and anti-platelet adhesion properties are studied.

2. Experimental

2.1. Chemicals

Cis-cyclooctene (99%) is purchased from Acros Organics Co. Ltd. Lithium aluminum hydride (98.3%) and m-chloroperoxybenzoic acid (mCPBA) (85.3%) are purchased from Tianjin Hainachuan Science and Technology Company. 1,5-Cyclooctadiene (99%), 1-hexene (97%), ethyl vinyl ether (99%) and Grubbs' generation II catalyst are purchased from Aldrich. Toluene diisocyanate (TDI) is purchased from Wuhan Zhongtian Chemical Reagent Co. Ltd. Poly(ethylene glycol) methyl ether (Mn = 350, 550, 750, 1000) is obtained from Alfa Aesar. Tetrahydrofuran (THF) is distilled with sodium and ketyl benzophenone, and dichloromethane is distilled with calcium hydride. The protein, bovine serum albumin (BSA), is obtained from Beijing Dingguo Biotech. Co. Ltd.

2.2. Polymerization procedure

The preparation of cyclooctene-PEG macromonomer and PCOE-g-PEG copolymer was following the method used in our previous paper [21]. The solution of polyethylene glycol monomethyl ether (MPEG) (0.0042 mol) in 10 mL of toluene was dropwise added into a solution of TDI (0.004 mol) in 10 mL of toluene within 1 h at 40 °C under argon atmosphere. The system was kept at 40 °Cfor 24 h to yield MPEG-TDI. Then the temperature was elevated to 90 °C and 5-hydroxy-1-cyclooctene (0.004 mol) in 10 mL toluene was added slowly into the system within 1 h under argon atmosphere. The reaction was kept at 90 °C for another 24 h to obtain cyclooctene-PEG macromonomer. The yield of cyclooctene-PEG macromonomer is approximately 60%. Certain amount of cyclooctene-PEG and cyclooctene was dissolved in anhydrous dichloromethane (0.8 mL) and added in a dry Schlenk tube under argon. In another vial, Grubbs' generation II catalyst (4 μmol) was dissolved with anhydrous dichloromethane (0.2 mL). Both systems were subjected to freeze/pump/thaw cycles twice. Consequently, the catalyst solution was added rapidly into the monomer solution and the reaction would be kept at ambient temperature (25 °C) for 5 h with magnetic stirring. Then 1 mL ethyl vinyl ether was utilized to terminate

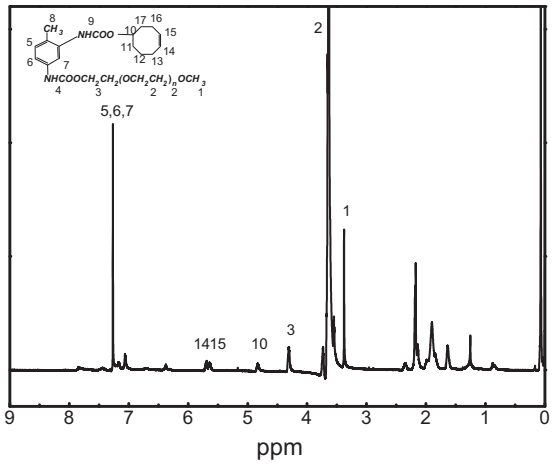

Fig. 2. ^{1}H-NMR spectrum of cyclooctene-PEG(750) macromonomer.

the polymerization and dichloromethane to dilute the polymer solution. The as-synthesis product was then precipitated into methanol containing 0.01 wt.% butyrate hydroxyl toluene (BHT) [22]. Thereafter, the precipitate would be dried under vacuum at room temperature to prevent the cross-linking of un-saturated double bonds in polyolefin main chain after filtration, and 0.12 g (70.9% yield) off-white solid was obtained.

2.3. The preparation of PCOE-g-PEG film

Surfaces for X-ray photoelectron spectroscopy, atomic force microscopy, contact angle measurement, BSA protein adsorption and platelet adhesion testing were prepared on glass slide by spin-coating 0.5% (w/w) solutions of PCOE-g-PEG graft copolymers in dichloromethane at 2000 rpm for 30 s using a KW-4A spin coater. Then the surfaces of the samples prepared for measurement were dried in a vacuum oven at reduced pressure at room temperature for at least 12 h to remove solvent completely. The thickness of the film is about 150 nm.

2.4. Characterization

Fourier transform infrared (FTIR) spectroscopy was performed on the Spectrum one NTS spectrometer from Perkin-Elmer Corporation. The spectra were recorded from 500 to 4000 cm^{-1} in the absorbance mode. ^{1}H NMR spectra were recorded using a UNITY INOVA 600 MHz Spectrometer (Varian Company Ltd.) at room temperature with TMS

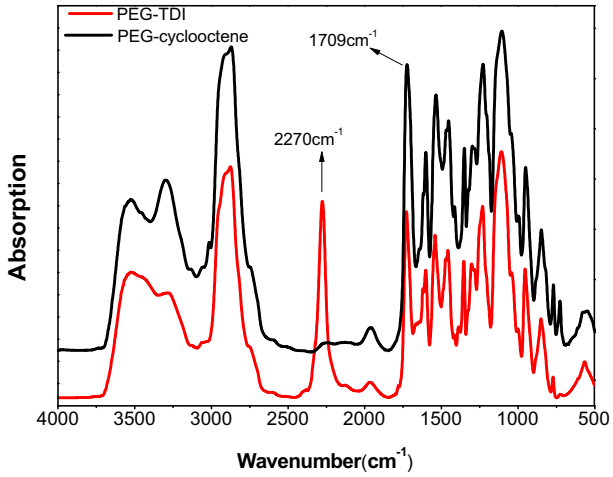

Fig. 1. FTIR spectra of PEG-TDI and cyclooctene-PEG(750) macromonomer.

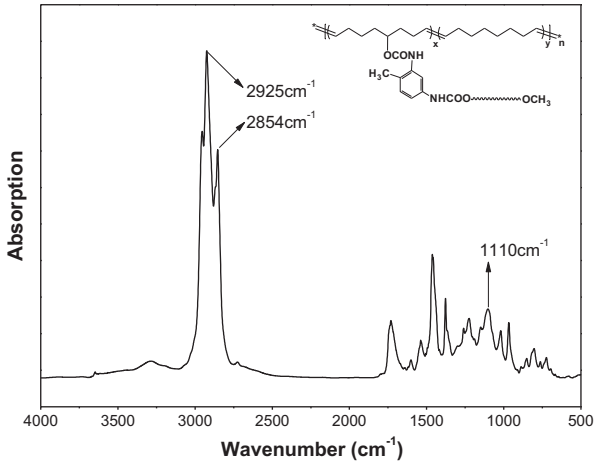

Fig. 3. FTIR spectrum of PCOE-g-PEG(750) copolymer.