Colloids and Surfaces B: Biointerfaces 161 (2018) 73–82

Contents lists available at ScienceDirect

Colloids and Surfaces B: Biointerfaces

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

Full Length Article

Surface modification of polyisobutylene via grafting amino acid-based poly (acryloyl-6-aminocaproic acid) as multifunctional material

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ARTICLE INFO

Article history:
Received 14 June 2017
Received in revised form 7 September 2017
Accepted 11 October 2017
Available online 12 October 2017

Keywords:
Polyisobutylene
Poly (acryloyl-6-aminocaproic acid)
Hemocompatibility
Concanavalin A
Erythrocyte

ABSTRACT

Amino acid-based P(acryloyl-6-aminocaproic acid) (PAACA) brushes were fabricated on polyisobutylene (PIB) surface combined with plasma pre-treatment and UV-induced grafting polymerization to construct an antifouling and functional material. The hydrophilicity and hemocompatibility of PIB were largely improved by surface modification of AACA, which were confirmed by water contact angle and platelet adhesion, respectively. PAACA brushes were precisely located onto the surface of PIB to create a patterned PIB-g-PAACA structure, and then the carboxyl groups on PAACA was activated to immobilize functional protein-Concanavalin A (Con A). The obtained Con A-coupled microdomains could further capture erythrocytes. This method developed a platform on commercial PIB surface via amino acid-based polymer brushes which had a promising application in drug delivery and disease diagnosis.

1. Introduction

Polyisobutylene (PIB) is a specialty polymer which can be obtained by the cationic polymerization of isobutylene [1]. It has unique properties such as low permeability, excellent oxidative and thermal stability, high hysteresis (mechanical dampening), and tack [2]. Butyl rubber is developed due to the discovery of low permeability and has been used in many fields including tires, vibration dampeners, railway pads, tank liners and cable coating. Besides, PIB-based materials are prepared for biomedical applications. Both conventional and living carbocationic polymerizations have been used to develop PIB-based biomaterials [3–6]. The viscoelastic properties of PIB combined with cyanoacrylate chemistry provided the probability to design a new synthetic material using in intervertebral disk replacement [7].

Both PIB and non-crosslinked butyl elastomers are approved by the Food and Drug Administration for the chewing-gum base and other food-related applications. Crosslinked butyl rubber is also used in blood bags and pharmaceutical stoppers due to its excellent barrier properties. PIB-based materials also have potential application in immunoisolatory membranes [8–11] and vascular grafts [12]. Surface properties play an important role on the hemocompatibility of biomaterials [13]. The hydrophobic property of PIB promotes plasma protein adsorption, induces platelets adhere, spread, and aggregate, ultimately leading to thrombus formation [14]. Several strategies have been used to modify biomaterials surfaces, such as physical absorption [15,16], plasma discharge [17,18], γ-ray irradiation [19,20], surface-initiated atom transfer radical polymerization [21–23], and UV-induced surface graft polymerization [24,25]. UV-induced surface graft polymerization is attractive because of its easy operation, simple equipment, low cost, and mild reaction conditions. Puskas et al. demonstrated that E. coli attachment to 29 kDa protein-coated PIB-PS in vitro was reduced by 90% [26]. However, few studies have improved the hemocompatibility of PIB by grafting hydrophilic polymers or constructed functional surface. Some grafting brushes, such as oligoethylene glycol (OEG)- or polyethylene glycol (PEG)-based monomers [27], amphiphiles [28], zwitterionic polymers [29–31], biomacromolecules [32,33], have been used for improving hemocompatibility of biomaterials. The inclusion of amino acids in polymeric compositions has been proved to achieve desirable properties in many biomedical applications. Therefore, amino acid-derived monomers have drawn the most attention [34–36]. Acryloyl-6-aminocaproic acid (AACA) with flexible-pendant side chains carrying an optimal

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https://doi.org/10.1016/j.colsurfb.2017.10.035
0927-7765/

balance of hydrophilic represents an exciting class of smart, easy-to-synthesize materials with widespread potential applications in biology and medicine. Cong et al. [37] have prepared a novel class of graphene oxide (GO)/poly(acryloyl-6-aminocaproic acid) (PAACA) composite hydrogels with enhanced mechanical properties and self-healing capability to pH stimulus. Mashelkar et al. also synthesized self-healing hydrogels formulated from AACA precursors which possessed an optimal balance between hydrophobic and hydrophilic interactions [38]. Moreover, the carboxyl group in AACA provides reactive points to immobilize biomacromolecules, such as immunoglobulin, polysaccharides, and enzyme by EDC/NHS chemistry. Specificity and selectivity of a platform are the two criteria to immobilize target biomacromolecules in the successful development of biosensors [39]. Polymer brushes that are tethered on a substrate and extended polymer chains with freedom in solution offer a promising supporting layer to immobilize or detect biomacromolecules.

In this study, AACA was synthesized and grafted onto the surface of PIB by plasma pre-treatment and UV-induced graft polymerization. The structure of polymer brushes was examined by attenuated total reflectance Fourier transform infrared spectroscopy (ATR-FTIR) and X-ray photoelectron spectroscopy (XPS). The wettability and surface energy of modified PIB were assessed by static water contact angle measurements. The antifouling property was investigated by protein adsorption and platelet adhesion. Concanavalin A (Con A) was used as a model protein and immobilized onto the surface of PIB by activating carboxyl group to capture red blood cell (RBC). RBCs capturing confirmed the activity of Con A and the potential application of modified PIB in protein immobilization and development of biosensors.

2. Experimental

2.1. Materials

PIB granules were obtained from China Petroleum & Chemical and pressed into films by plate vulcanizing press. The obtained films were approximately 1 mm thick. Acryloyl chloride, 6-aminocaproic acid, *N*-(3-dimethyl aminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC), and N-hydroxysuccinimide (NHS) were purchased from Aladdin chemical Co. Benzophenone (BP), Concanavalin A (Con A), and fluorescein isothiocyanate labelled Con A (FITC-Con A) were purchased from Sigma-Aldrich chemical Co. Fluorescein isothiocyanate labelled fibrinogen (FITC-Fib) and rhodamine labelled bovine serum albumin (RBITC-BSA) were obtained from Bioss. Inc. Phosphate-buffered saline (PBS, 0.01 M phosphate buffer, pH 7.4) was freshly prepared, which was used for protein adsorption, platelet adhesion, and immobilization of Con A experiments. The other solvents and reagents were AR grade and used without further purification.

2.2. Synthesis of AACA

The AACA monomers were synthesized and characterized as described elsewhere [14,40]. Briefly, 0.1 mol 6-aminocaproic acid and 0.11 mol NaOH were dissolved in 80 mL deionized water in an ice bath under vigorous stirring. To this, 0.11 mol acryloyl chloride in 15 mL tetrahydrofuran was added dropwise. The pH was maintained at 7.5–7.8 until the reaction was completed. The reaction mixture was then extracted with ethyl acetate. The clear aqueous layer was acidified to pH 3.0 and then extracted again with ethyl acetate. The organic layers were collected, combined, and dried over sodium sulfate. The solution was then filtered, concentrated, and precipitated in petroleum ether. Further purification was achieved by repeated precipitation, and the product was lyophilized. The structure of AACA was examined by ^{1}HNMR in $CDCl_3$ and ^{13}CNMR in $(CD_3)_2SO$.

2.3. Surface grafting of AACA

The PIB films were washed with ethanol and deionized water and then dried under vacuum for 24 h at room temperature before use. After that, oxygen plasma pre-treatment was conducted using DT-03 plasma apparatus (Suzhou Omega Technology Co., Ltd) for 120 s. Subsequently, the film was coated with 1 wt% solution of BP and quartz plate was covered with the film. The sandwiched system was exposed to UV light (high-pressure mercury lamp, 400 W, main wavelength 380 nm) for 3 min. The BP modified films were washed with ethanol and dried under nitrogen. After that, the BP modified film was coated with 0.5 wt% solution of AACA. A metal photomask was put on the PIB surface, and quartz plate was covered with the film. Finally, the sandwiched system was exposed to UV light for the desired period. All the films were cleaned with ethanol and deionized water to remove residual monomer, followed by drying in a vacuum oven for 24 h. The grafting density of PIB-g-PAACA was calculated by the following equation:

$$\text{Grafting Density}(\mu g/\text{cm}^2) = \frac{W_1 - W_0}{A_0}$$

where W_0 and W_1 represent the weight of pristine and modified PIB films, respectively; A_0 represents the area of the films. The weight gain was measured by an analytical balance, and the accuracy is 0.01 mg. All the obtained results were the average of three parallel experiments.

2.4. Immobilized of Con A

The modified PIB film was activated in 0.4 M EDC and 0.1 M NHS for 1 h at 4 °C, and then washed twice with PBS and equilibrated in 0.1 M MES. 50 μL 0.1 mg/mL Con A-PBS solution was added onto the activated film for 12 h. After washed with PBS three times, the Con A conjugated PIB film was fabricated.

2.5. Characterization

The surface chemical structure of the modified PIB films was analyzed by FTIR (BRUKER Vertex 70) with an ATR unit (attenuated total reflection crystal, 45°) at a resolution of 4 cm^{-1} for 32 scans. The chemical composition of modified PIB films was characterized by XPS (VG Scientific ESCA MK II Thermo Avantage V 3.20 analyzer) with Al/K ($h\nu$ = 1486.6 eV) anode mono-X-ray source. All the samples were completely vacuum dried before use. The releasing angle of the photoelectron for each atom was fixed at 90°. Surface spectra were collected over a range of 0–1200 eV, and high-resolution spectra of C1s, N1s, and O1s regions were collected. The atomic concentrations of the elements were calculated by their corresponding peak areas.

2.6. Static water contact angle and surface energy

The static water contact angles (WCA) on the surfaces of PIB films was measured using a contact angle goniometer (DSA, KRUSS GMBH, Germany) by the sessile drop method with a 2 μL water droplet. The WCA values were recorded after 3 s from droplet deposition. For each value reported, at least five measurements taken from different surface locations were averaged. The surface energy of PIB film was then calculated according to the following equation:

$$\cos\theta = -1 + 2\sqrt{\gamma_s/\gamma_l}\exp\left[-\beta(\gamma_s - \gamma_l)^2\right]$$