Materials Science and Engineering C 58 (2016) 133–141

Contents lists available at ScienceDirect

Materials Science and Engineering C

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

Improving blood-compatibility via surface heparin-immobilization based on a liquid crystalline matrix

Jupeng Zhao [a,b,1], Yang Chen [a,b,1], Shenyu Yang [a,b], Shaopeng Wu [a,b], Rong Zeng [a,b], Hao Wu [c], Jiaqing Zhang [d], Zhengang Zha [c], Mei Tu [a,b,*]

[a] Department of Materials Science and Engineering, Jinan University, Guangzhou 510632, PR China
[b] Engineering Research Center of Artificial Organs and Materials, Ministry of Education, Jinan University, Guangzhou 510632, PR China
[c] The First Affiliated Hospital, Jinan University, Guangzhou 510632, PR China
[d] School of Medicine, Jinan University, Guangzhou 510632, PR China

ARTICLE INFO

Article history:
Received 12 May 2015
Received in revised form 24 July 2015
Accepted 14 August 2015
Available online 20 August 2015

Keywords:
Heparin
Liquid crystal
Blood compatibility
Surface modification

ABSTRACT

Blood compatibility is of considerable importance in developing medical materials and devices that are in contact with blood. In this work, we successfully developed a novel liquid crystalline heparin-immobilized material (Hep-OPPC) by two-step modification for further improvement of hydrophilicity and hemocompatibility of the liquid crystalline hydroxypropyl cellulose ester (OPC_L). The results showed that Hep-immobilization on the OPC_L led to dramatic changes in the surface morphology and crystallinity, whereas, the Hep-OPPCs also maintained the liquid crystalline feature at room temperature after heparinization. Furthermore, the hemocompatibility of the Hep-OPPCs was markedly enhanced at low levels of hemolysis assay (HR) with unimpaired erythrocytomorphology, significantly lower concentrations of C3a in blood plasma and remarkable increases in plasma re-calcification time (PRT). This suggests that the heparinized surface could restrict the transformation of fibrinogen with less activation of the intrinsic coagulation system. Moreover, the activated partial thromboplastin time (APTT) and prothrombin time (PT) values of the Hep-OPPCs with low heparin density could also be prolonged in this study suggesting that the liquid crystal feature of the matrix might be blocking the clotting factors. We concluded that the heparin-immobilized liquid crystalline material has the potential to be used in blood-contact materials.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Hemocompatibility is very essential for blood-contacting medical devices such as artificial heart valves, vascular stents and ventricular assist devices [1,2] because coagulation and thrombosis are major risks. Many efforts have been employed to mimic the composition and properties of the native cardiovascular environment [2–7].The design and construction of liquid crystalline surfaces are now considered an effective way to improve the blood compatibility of various materials [5,8–11].

The liquid-crystalline state is widely found in many biological systems. For example, cell membranes, phospholipids, proteins, cholesterols and DNA are known to exist in liquid-crystal phases [12–14]. Moreover, the inner surface of blood vessels has been shown to be a mobile liquid crystal [15]. Liquid crystal molecules can behave like mobile plasma membranes due to their phase transition properties, which makes them biocompatible and useful as anticoagulant components [16]. Shih et al. suggested that liquid crystal-embedded polymers could decrease the platelet activation to improve blood compatibility [17] indicating that the'sensing'liquid crystal (LC) material might become an active substrate for the biological material [18] lying in liquid crystalline phase while providing more molecular mobility for binding interactions with cells [19].

In our previous studies [16,20], a series of small molecular LCs (mainly cholesteryl tetraethylene glycol carbonate), polymer LCs (mainly hydroxypropyl cellulose ester) and various polymer/LC composite membranes were prepared to explore their blood compatibility. The results showed that polymer liquid crystals had better stability than small molecular ones and thus were more useful in biomedical applications. Furthermore, the blood compatibility of these polymers was improved by being embedded into a certain proportion of LC [21]. For example, a polysiloxane/liquid crystal composite membrane with 20–30% (wt) LC offered much better blood compatibility than the others [16], which indicated that the embedded liquid crystal phase possibly exerted strong influences on the hemocompatibility of the polymer materials. However, the hydrophobicity and potential activation of

* Corresponding author at: Department of Material Science and Engineering, College of Science and Engineering, Jinan University, 601 Huangpu Avenue West, Guangzhou 510632, PR China.
E-mail address: tumei@jnu.edu.cn (M. Tu).
[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.msec.2015.08.025
0928-4931/© 2015 Elsevier B.V. All rights reserved.

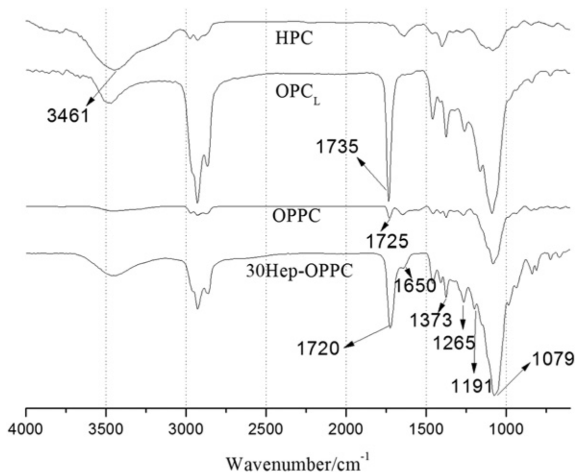

Fig. 1. ATR-FT-IR spectra of HPC and its modified membranes.

complement C3 limited their biomedical applications, because the hydrophobicity of biomaterials is an important determinant for the blood cells' membrane-disruptive activity [22], hydroxyl groups from the hydroxypropyl cellulose ester-based liquid crystalline materials probably led to the activation of complement C3 [23]. To address this problem, it is essential to further enhance the biocompatibility of these liquid crystalline materials. This will broaden their applications as a coating for long-term implantation of biomedical devices.

It is well known that immobilization of heparin molecules onto the material surface is an effective strategy for minimizing the thrombogenicity of materials [11,24] via their specific interaction with antithrombin III (AT III). This not only suppresses the conversion reaction from fibrinogen to fibrin, but also prevents platelet adhesion and aggregation [25]. Based on the idea of surface heparinization, we developed novel types of heparin-immobilized liquid crystalline materials that could serve as blood-compatible biomaterials. Here, the heparinized surfaces have anticoagulant properties that increase blood clotting time. Moreover, the distribution of sulfonic, sulfo-amino, and carboxyl groups on the surface can markedly improve the hydrophilicity of this liquid crystalline material and lead to better biocompatibility. In this work, heparinized liquid crystalline hydroxypropyl cellulose ester was prepared via esterification of hydroxypropyl cellulose (HPC) followed by heparin-immobilization. We then characterized the surface morphology, crystalline behavior and blood compatibility of the heparinized materials.

2. Materials and methods

2.1. Materials

Hydroxypropyl cellulose (HPC, $M_w = 100{,}000$), octanoyl chloride, acryloyl chloride and heparin sodium (Hep, >150 IU/mg) were purchased from Sigma-Aldrich. PVC venous cannula (PVCvc, provided by Dong Guan Kewei Medical Instrument Co. Ltd, and had been in application in clinic)

2.2. Preparation of heparinized liquid crystalline hydroxypropyl cellulose ester

2.2.1. Synthesis of liquid crystalline hydroxypropyl cellulose ester

Hydroxypropyl cellulose ester (OPC_L) was prepared according to the developed method from previous works [26]. Briefly, HPC (3 g) was dissolved in 18 mL acetone with mild stirring followed by rapid addition of octanoyl chloride with a syringe. After 2 h of reflux at 55 °C, the reaction mixture was poured into 200 mL distilled water. After removing the liquid phase, the cream colored sticky mass was dialyzed in tetrahydrofuran (THF) to remove the residual octanoyl chloride and then dried at 60 °C (30 mbar, 48 h).

The OPC_L was dissolved in acetone and then added to acryloyl chloride with continuous stirring at 55 °C for 3 h. After the purification procedure described above, the product [octanoyl-, acryloyl-hydroxypropyl cellulose ester (OPPC)] was obtained.

2.2.2. Heparinization of liquid crystalline hydroxypropyl cellulose ester (Hep-OPPC)

The OPPC membranes were prepared via a solution-casting method. The OPPC membranes were first immersed in PBS solution for 24 h and then in a solution of Hep/NaOH at 5 mg/mL, 10 mg/mL, 30 mg/mL and 50 mg/mL for 4 h (samples were labeled as 5Hep-OPPC, 10Hep-OPPC, 30Hep-OPPC, and 50Hep-OPPC respectively). After that, the membranes were rinsed thoroughly with ultra-pure-water to remove physically adsorbed Hep from the OPPC surface and subsequently preserved in a dryer.

2.3. Measurement and analysis

2.3.1. Characterization

The surface composition was determined by attenuated total reflection-flourier transform infrared spectra (ATR-FTIR; Bruker EQUINOX-70, Germany) and an X-ray photoelectron spectrometer (XPS; ESCALAB 250, America). The surface texture was viewed by using a polarized optical microscopy (POM; XPL3230, China) equipped with a digital camera system. The surface morphology of the tested membranes was observed with a scanning electron microscopy (Philips XL-30ESEM, Netherlands) after sputter-coating a gold layer (BAL-TEC, SCD005). The membrane crystallization was measured with a Dmax-1200 diffractometer (XRD, Japan) using Cu Kα radiation generated with 30 kV and 20 mA. Five films were stacked in aluminum holders and scanned at room temperature over the 2θ range 5–40° at 8°/min. Data were recorded every 0.02°.

2.3.2. Determination of immobilized heparin

The samples with an area of 1 mm × 5 mm were incubated with 5 mL of toluidine blue/PBS and gently shaken for 4 h at room temperature. This resulted in a complex of toluidine blue with heparin. The complex was extracted with normal hexane, and the absorbance of subjacent blue solution was measured at 630 nm using an UV–Vis spectrophotometer. The calibration curve was obtained through measurement of the absorbance of a series of standards at heparin concentrations of 5–30 μg/mL. The amount of immobilized heparin was calculated from the calibration curve, and OPPC film was served as the control.

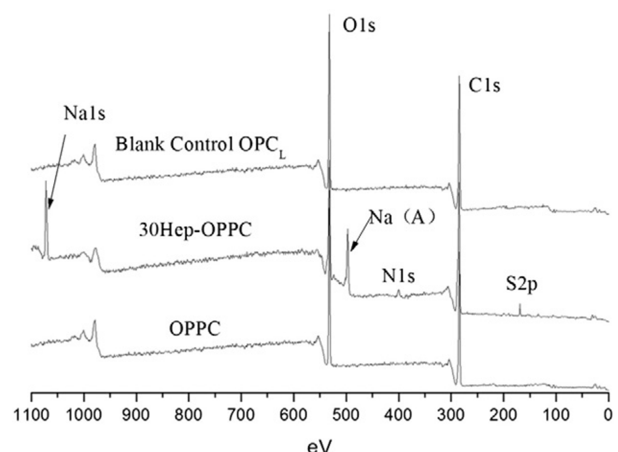

Fig. 2. XPS spectra of modified HPC membranes.

Download English Version:

https://daneshyari.com/en/article/7868395

Download Persian Version:

https://daneshyari.com/article/7868395

Daneshyari.com