Ultra-low fouling biocompatible polycarboxybetaine coatings

Kan Wu, Hsiang-Chieh Hung, Peng Zhang, Shaoyi Jiang.
Department of Chemical Engineering, University of Washington, Seattle, Washington 98195-1750.

Statement of Purpose: Demand for biocompatible non-fouling surfaces is increasing with the development of implantable medical devices, hemodialysis, biosensors, implantable chips, and drug delivery carriers [1] However, current hydrophilic polymers, such as poly (ethylene glycol) (PEG), have potentials to introduce immunological response or complement activations. Polycarboxybetaine (pCB) zwitterionic material, distinguishes itself by its super-hydrophilic and chemically stable nature. These features make it a promising, non-toxic and biocompatible non-fouling material. [2] However, the pretreating process of "graft-from" method impedes practical applications on bio-medical devices. Under this circumstance, a mussel-inspired catechol molecule was applied in this experiment for its universal-binding nature. [3] It is expected that the conjugation of dihydroxyphenylalanine (DOPA) molecules with a CB polymer will lead to an ideal surface-independent non-fouling coating material.

Methods: In this work, a unique pCB-DOPA conjugate with L-DOPA binding groups attached at the pCB chain end was designed and synthesized through atom transfer radical polymerization (ATRP). The immobilization of pCB-DOPA conjugate onto commonly used medical materials [e.g., polypropylene (PP), polyvinyl chloride (PVC), polystyrene (PS), polydimethylsiloxane (PDMS) and glass] was achieved by soaking substrates in a conjugate Tris solution (pH=8.5) with the concentration of 1.5mg/ml, followed by washing with DI water and dried with airflow. The hydrophilicity of surfaces after coating with conjugates was confirmed by measuring static contact angles in the air at room temperature using a contact angle goniometer (model 100-00-l 15, Ram&Hart, Succasunna, NJ, USA). X-ray photoelectron spectroscopy (XPS) was applied to demonstrate the successful coating of conjugates onto the substrates. The performance of coating on different surfaces was quantitatively studied by the enzyme-linked immunosorbent assay (ELISA) using protein-HRP conjugates.

Results. As shown in Figure 1a, the immobilized pCB zwitterionic layer significantly decreased the static contact angle of all treated surfaces down to a uniform 14±1, indicating that a phenomenal hydration layer was successfully formed by our zwitterionic coating. The existence of pCB-DOPA onto target surfaces was examined by XPS. PDMS was chosen as the substrate to testify the immobilization of conjugates on the surface. This is because nitrogen is the element contained only in the conjugates while not in bare PDMS, while silicon is the element that only exists in the PDMS substrate. The N1s/Si1s ratio from XPS survey scan can be used to demonstrate the successful coating of pCB-DOPA conjugates on PDMS. As shown in Figure 1b, the N/Si ratio increased from 0 (PDMS control) to around 0.4 (pCB-DOPA: 20 h incubation in Tris buffer). This directly confirmed the immobilization of a pCB layer on the surface.

The non-fouling ability of the coating layer was evaluated by measuring non-specific protein adsorption before and after coating using an established ELISA protocol. [4] O-phenylenediamine dihydrochloride (OPD) in 0.1 M citrate-phosphate buffer induced a chromogenic reaction in anti-human plasma HRP-Fibrinogen conjugate protein; These results demonstrate their versatile effectiveness of coating different surfaces. As shown in Figure 1c. A reduction of nonspecific protein fouling to 2.3%，3.9%，4.1%, 5.9%, and 10.4% was observed on PP, PVC, PS, PDMS and glass surfaces, respectively after these surfaces were treated with pCB-DOPA conjugates.

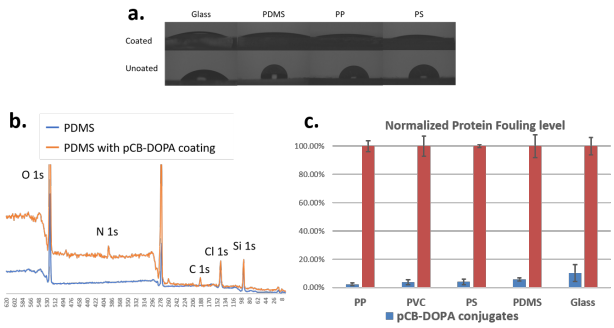

Figure 1. a) Contact angles of Glass, PDMS, PP, and PS. before and after coating. b) XPS survey scan of PDMS substrates before and after coating. c) ELISA measurement of protein adsorption on PS, PVC, PDMS and glass surface before and after pCB-DOPA treatments by ELISA.

Conclusions: To summarize, we demonstrated the non-fouling property of a zwitterionic pCB-DOPA conjugate onto different surfaces through a simple dip-coating procedure. The surfaces after coating were tested by a contact angle goniometer, XPS and a designed ELISA method. Results demonstrated that this dip-coating process is much simpler and more convenient than traditional Surface-initiated atom transfer radical polymerization (SI-ATRP) method. This pCB-DOPA conjugate successfully introduced a pCB zwitterionic layer immobilized on the tested surface and significantly increased the hydrophilicity of all tested surfaces regardless of their chemical nature. The pCB zwitterionic coating showed a significant non-fouling ability against protein fouling.

References: [1] W. Qiang, et al. Angewandte Chemie International Edition 2014, 53, 8004;
[2] S. Qing, Advanced Materials 2015, 27, 15.
[3] H. Lee, et al. Science 2007, 318, 426.
[4] H. S. Sundaram, et al. Advanced Materials Interfaces 2014, 1, 1400071.