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Glycocalyx-mimetic dextran-modified poly(vinyl amine) surfactant coating reduces platelet adhesion on medical-grade polycarbonate surface

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Abstract

A dextran-modified poly(vinyl amine) comb-like surfactant polymer, poly(*N*-vinyl dextran aldonamide-*co*-*N*-vinyl hexanamide), that can surface-adsorb on hydrophobic polymeric substrates, was designed to improve the interfacial blood-compatibility of polymeric biomaterials. Medical-grade polycarbonate was selected as a model substrate because of its extensive use in blood-contacting biomedical devices like hemodialyzers, blood pumps and oxygenators. The surfactant polymer was physisorbed from aqueous solution onto the polycarbonate substrate. The surfactant coating was stable under dynamic shear conditions in whole blood, as confirmed by fluorescence microscopy and total internal reflection fluorescence (TIRF) experiments with fluorescein-labeled surfactant polymer. The coated disks and uncoated control disks were exposed to platelet-rich plasma (PRP) and whole human blood in a rotating disk system (RDS) to study platelet-adhesion under dynamic shear stress environments. Adhered platelets were stained with fluorescein isothiocyante (FITC)-tagged anti-CD41a monoclonal antibody and imaged by epifluorescence microscopy. Complimentary images were obtained by phase-contrast microscopy. Platelet adhesion on the surfactant-coated disks was reduced by ~90%, compared with uncoated disks. The images also showed a concomitant reduction in platelet-derived microparticles on surfactant-coated disks, compared with uncoated disks. The results suggest potential application of carbohydrate-modified surfactant polymers as a glycocalyx-mimetic non-thrombogenic interfacial coating for blood-contacting biomaterials.

Keywords: Glycocalyx-mimetic; Interface; Blood-compatibility; Coating; Platelet adhesion

1. Introduction

All synthetic materials used in blood-contacting medical devices promote surface-induced thrombotic phenomena to various extents. These events are initiated by non-specific protein adsorption followed by platelet adhesion, activation and aggregation, on the biomaterial surface [1–4]. The resulting thrombus can impair the function of the implanted devices, while thromboembolic events can occlude blood vessels leading to serious cardiovascular complications. Hence, non-thrombogenicity is a highly desired surface property for blood-contacting biomaterials. Modification of a biomaterial surface with a chemical or a biological substance that can reduce/prevent surface-adhesion phenomena when exposed to blood proteins and cells has become an important strategy to induce non-thrombogenicity, and its clinical importance has been the driving force for numerous studies [5–8]. Current surface modification methods include physico-chemical (e.g. plasma/ion-beam modification and etching) processes, polymer grafting (e.g. PEG or sulphobetaine modification),

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physisorption/self-assembly processes (e.g. alkanethiols SAMs) and biological methods (e.g. heparin grafting, hirudin immobilization and endothelialization) [5–16]. Even though various surface treatments have generally improved blood compatibility, major advances in clinical applications have yet to be realized. Our approach to this problem, employing surface assembling surfactant polymers [17,18] is to design interface materials based on mimicking the cell glycocalyx.

The physisorption/self-assembly method has generated particular interest with respect to surface-modification of hydrophobic polymeric biomaterials with glycocalyx-mimetic surfactant polymers [19,20]. The endothelial glycocalyx, a hydrated structure rich in proteoglycans, glycosaminoglycans and other glycosylated molecules [19–23], plays a significant role in maintaining the non-adhesive/non-thrombogenic property of the native intravascular luminal wall. Mimicking this carbohydrate-rich structure on a biomaterial provides a route towards suppressing biomaterial-induced thrombotic events. Based on this rationale, carbohydrate-modified poly(vinyl amine) surfactant polymers have been developed that adsorb spontaneously on a variety of biomaterials surfaces forming a thermodynamically driven surface-coating. Here, we report the efficacy of a glycocalyx-like surfactant polymer coating towards preventing platelet adhesion and aggregation from plasma and whole blood under a dynamic shear environment. We have chosen medical-grade polycarbonate as a model substrate since, it has extensive applications in a variety of blood-contacting biomaterial devices including hemodialyzers, blood pumps and oxygenators and blood filters.

2. Materials and experimental methods

2.1. Surfactant polymer synthesis

Low-molecular weight (M_n~6000 Da) poly(vinyl amine) (PVAm) with well-defined structure and low polydispersity was synthesized from poly(*N*-vinylformamide) according to previously published procedures [24–29]. All chemical reagents and solvents were obtained from Sigma-Aldrich-Fluka (St. Louis, MO). The PVAm was derivatized by reaction with *N*-(hexanoyloxy)succinimide and dextran lactone, to yield pendant hexanoyl and dextran aldonamide groups on the PVAm backbone (Fig. 1A). The ratio of dextran aldonamide to hexanoyl groups on the

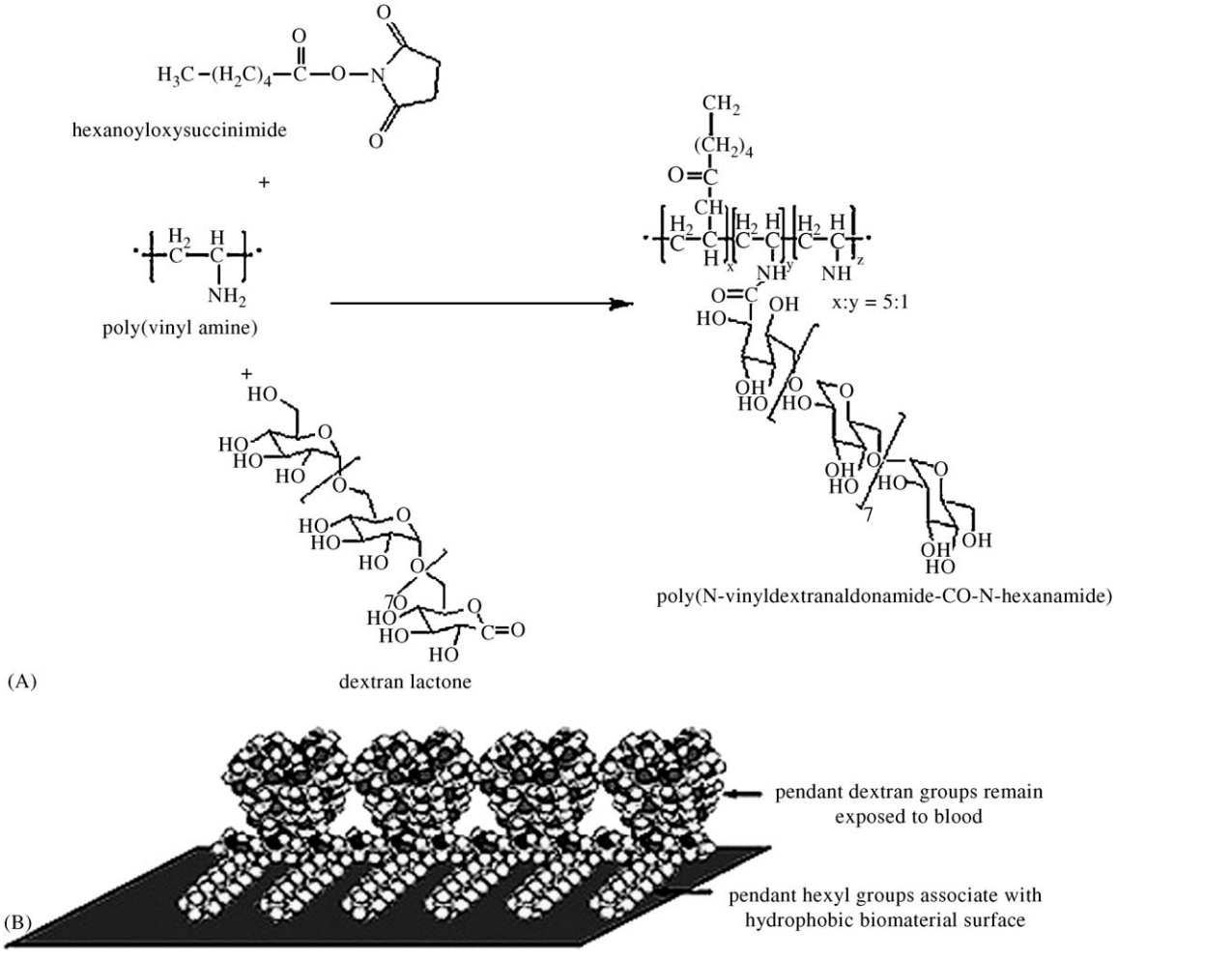

Fig. 1. Glycocalyx-mimetic poly(vinyl amine) surfactant polymer; (A) shows the synthesis scheme for the dextran-modified surfactant polymer. (B) shows a molecular model schematic of the surfactant adsorption on a hydrophobic surface.