Surface fluorination of polylactides for enhanced hemocompatibility

Razieh Khalifehzadeh[1], Buddy D. Ratner[1,2]
[1] Department of Chemical Engineering, University of Washington-Seattle
[2] Department of Bioengineering, University of Washington-Seattle

Statement of Purpose: Surface-induced thrombosis by biomaterials remains a significant clinical concern for many types of blood-contacting medical devices (*1*). In particular, protein adsorption and platelet adhesion are important events due to their ability to trigger the coagulation cascade and initiate thrombosis (*2*). Fluorocarbon treatment has been shown to decrease platelet adhesion despite the presence of fibrinogen (Fg) on the biomaterials surfaces (*3*). In addition, hydrophobic fluoropolymers that have shown good clinical performance exhibit high albumin adsorption level and tight binding of proteins (*4*).

Polylactide (PLA) has been the predominant polymer used for making bioresorbable stents. USFDA has recently approved the first fully absorbable stent manufactured from PLA to treat coronary artery disease. Although bioresorbable stents have various long-term advantages, they are associated with higher rates of thrombosis compared with permanent metallic stents.

To address this issue, we modified the surface of PLA with a perfluoro compound facilitated by surface activation using radio frequency (RF) plasma. The compositions of modified surfaces and relevant blood compatibility parameters, including plasma protein adsorption, platelet adhesion and morphology, were evaluated.

Methods: We prepared 8mm PLA pellets and placed them in a in a radio-frequency glow discharge plasma reactor to introduce amine functionalities to their surfaces. The polymer pellets were placed on a glass rack and ammonia was introduced into the reactor at a controlled flow rate of 1.4 sccm. We applied 40 W generator power for 2 min for all PLA samples. Under the same experimental conditions, both sides of the PLA pellets were activated. Then amino-activated PLA samples were placed into scintillation vials and filled with 1ml of 10% (v/v) of 1,1,1-trifluoro-3-isocyanatopropane (TFICP) solution in dry Hexane. After 2 h incubation at room temperature, reaction mixture was removed and samples were rinsed with copious amount of Milli-Q water and dried in desiccator overnight.

Two proteins implicated in thrombosis were radiolabeled with I-125 to allow quantification of the protein adsorption to the fluorinated PLA surface. Fg and albumin (Alb) labeling was accomplished by using a modified iodine monochloride (ICl) technique with a 2:1 molar ratio of ICl to Fg and 3:1 molar ratio of ICL to Alb (*4*). Any excess I-125 was separated from the labeled protein using a gel filtration column. Protein adsorption was performed for 2h at 37°C in a solution of buffer and human blood plasma.

Results: The compositions of modified surfaces determined by electron spectroscopy for chemical analysis (ESCA). Scan survey of fluorinated samples (PLA-F) showed the presence of F in addition to C, O and N indicating successful integration of TFICP onto the surface of these samples. Contact angle measurements showed the higher hydrophobicity of the fluorinated surfaces, which is desirable for blood contacting materials. The Alb adsorption amounts were relatively greater for the fluorinated samples and it decreased in the order of PLA-F > PLA > PLA-NH_2 > 316ss. After elution with 2% sodium dodecyl sulfate (SDS), a greater amount of Alb was retained on PLA-F as compared to all other samples tested (Figure 1).

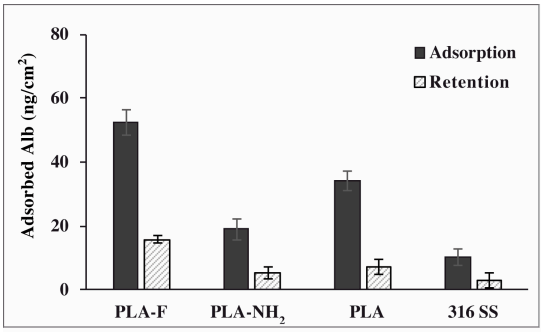

Figure 1. Alb adsorption from 1% citrated normal human plasma. The amount of retained protein on the surfaces was measured after 24 h incubation with 2% SDS.

Conclusions: We have established a novel approach for functionalizing PLA with trifluoromethyl groups to improve its hemocompatibility. TFICP immobilized surfaces had higher hydrophobicity and showed no sign of cytotoxicity toward NIH-3T3 fibroblast cells. So far, we have seen differentiated protein adsorption behavior of fluorinated PLA compared to control samples. TFICP immobilized surfaces adsorbed higher amount of the Alb in human blood plasma solutions. In addition, we observed greater amount of retained Alb on these surfaces after incubating them with 2% SDS. We therefore would expect these fluorinated surfaces to show improved blood compatibility in vivo as tight binding of Alb contributes to improved blood compatibility by passivating the surfaces of these polymers. Since a preadsorbed layer of Alb inhibits subsequent adhesion of Fg and decreases platelet adhesion producing a potentially less thrombogenic surfaces (*5*). In fact, fluorinated surfaces have shown satisfactory clinical performance and have often been the material of choice for blood contact applications. Interaction of platelets with these fluorinated surfaces are currently under investigation.

References:

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