Development of a platelet friendly, infection-resistant storage device to extend shelf-life and improve transfusion safety

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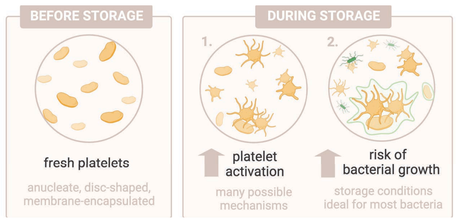
INTRODUCTION

Platelet transfusion is a lifesaving therapy to prevent and control bleeding in surgery, trauma, cancer, and other hematologic conditions.[1] Throughout their storage period of 5-7 days in polyvinylchloride (PVC) based devices, all platelet concentrates experience deleterious changes in structure and function, causing poor transfusion efficiency.

The hydrophobic PVC surface plays a major role in the deterioration of platelet quality, as it induces platelet adhesion, activation, and lysis.[2] Another factor limiting platelet shelf-life is room temperature storage, which create ideal conditions for the growth of most bacterial species.[3] Despite rigorous screening and testing procedures, 1 in 3000 platelet units is contaminated with bacteria, which can cause fatal transfusion reactions.



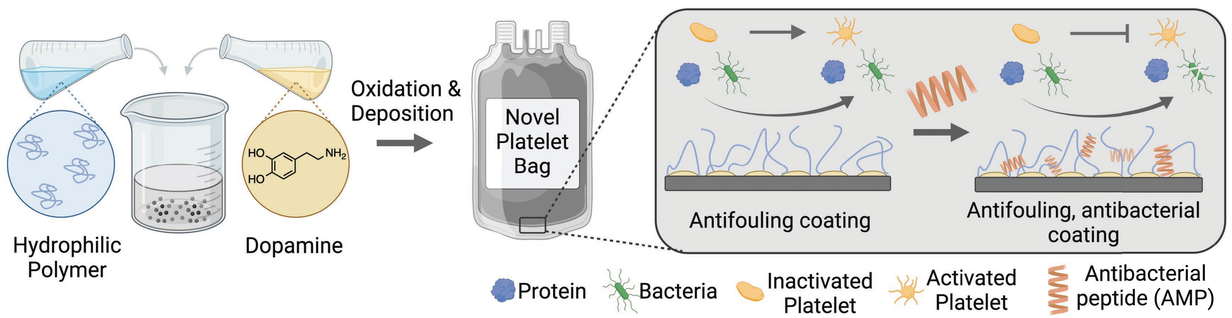
There is an unmet clinical need for improved storage devices that combat bacterial contamination and preserve platelet quality. Our strategy is to modify the storage device surface using platelet-friendly coatings as surface interactions play a large role in the loss of platelet quality and the risk of bacterial growth. We aim to develop a coating that is platelet friendly, resistant to bacterial growth, and adaptable to different commercial platelet storage containers without affecting their properties.

METHODS

A library of coatings based on polydopamine (PDA) and ultra-high molecular weight polymers (uHMWPs) were synthesized via a one-step deposition step in water. Platelet and bacteria adhesion tests were evaluated using the lactase dehydrogenase assay and colony forming unit (CFU) measurements, respectively.

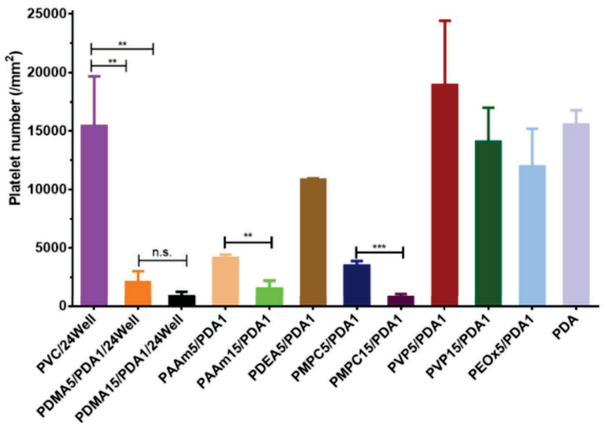
Cysteine end-functionalized antimicrobial peptides (AMPs) were tethered on the polymer coating via a Michael-type addition reaction between –SH groups on the peptides and quinone moieties on the coating. Platelet and bacterial adhesion, antimicrobial activity, and compatibility with stored platelets (platelet metabolism, activation marker CD62P, and clotting activity) were re-assessed to determine the optimal AMP-polymer combinations, ratios, and densities for platelet storage devices.

APPROACH



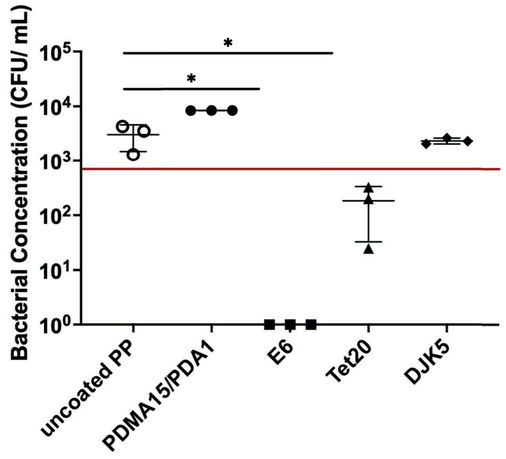
PRELIMINARY RESULTS

1. Platelet adhesion of the coating library with various hydrophilic polymers and at different dopamine: polymer ratios



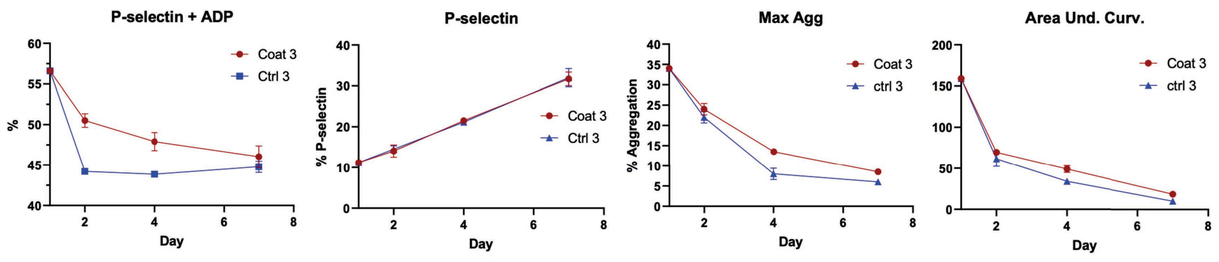
Platelet adhesion on uncoated and coated PVC following 4-hour incubation in platelet rich plasma. PDMA, PAAm, and PMPC at ratios of 15:1 polymer: dopamine reduced platelet adhesion by over 90% ($p < 0.01$). Student's two-tailed unpaired t-test was used for statistical analysis. *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

2. Antibacterial activity of three different AMP-conjugated PDMA/PDA coatings



Planktonic growth *S. epidermidis* in PDMA15/PDA1-coated polypropylene (PP) 96-well plates conjugated with three different antimicrobial peptides. Coatings conjugated with E6 and Tet20 reduced bacterial growth by 100% and 94%, respectively. Student's two-tailed unpaired t-test was used for statistical analysis. *$p < 0.05$.

3. Measurement of platelet activation in coated and uncoated PVC bags during storage



Platelet activation via expression of P-selectin (CD62p) and clotting activity in uncoated and PDMA15/PDA1-coated PVC bags over a 7-day storage period.

CONCLUSION & FUTURE WORK

The combination of non-fouling hydrophilic polymers and AMPs enables bifunctional coatings that may address the problems causing short shelf-life in platelet units. Preliminary results showed that coatings based on PDA and PDMA are effective at reducing platelet adhesion. Further conjugation with AMPs introduces antibacterial activity.

Next, we will screen a library of AMPs with different hydrophilic polymer based anti-fouling backgrounds to determine the optimal combination that prevent bacterial growth, platelet adhesion and subsequent activation.

The coating method introduced in this work will facilitate the development of platelet storage devices that resist platelet and bacterial adhesion, and prevent bacterial growth. This could alleviate platelet shortages, reduce wastage, increase transfusion safety, and improve hemostatic efficacy of platelets post-transfusion.

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