Riboflavin Plastic Modification for Antimicrobial Treatment

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Introduction

Biomedical devices are a +$400 billion market worldwide. Those range from single-use band-aids to highly sophisticated imaging devices. With yearly increased demand, safety for humans is of utmost importance for biomedical devices. This especially applies to plastics that make ≈50% of the global market of medical polymers for use in humans. Poly vinyl chloride (IUPAC name Poly(1-chloroethylene), a.k.a. PVC) ranks in third place as the most produced polymer worldwide and is the number one plastic in medical devices. PVC can be found in a wide variety of products from saline and blood bags to intracorporeal catheters.

While the inertness of PVC is an advantage for biomedical uses, surface modification to incorporate antimicrobial and antiviral moieties are challenging. Furthermore, susceptibility to microorganisms and viral contamination remains a long-standing issue for polymers, with 7.5% of patients experiencing healthcare-associated infections associated with surgeries and biomedical devices in Canada, and +50,000 lives are lost across the US and Europe due to multidrug resistance microorganisms.

Riboflavin (Rf), also known as vitamin B2, is a natural co-factor with photosensitizer capabilities in living organisms. Rf is approved as a nutritional supplement in many countries and has received FDA approval as a photo-therapeutic drug in keratoconus disease. In 2008, an Rf and UV irradiation technology was developed by Terumo® for blood bags (Mirasol® PRT System). This application is, however, limited where UV is not contraindicated as a potential hazard.

In this work, we report a cost-effective surface modification protocol for rapid attachment of Rf to PVC surfaces (see Figure 1). We produced antimicrobial and antiviral PVC surfaces that are hemocompatible, biocompatible, and remotely activated with low-energy blue light for microorganism eradication.

Results

Table 1. Physical and mechanical characterization of treated PVC plastics. n = 3 for each measurement. Values = mean ± SD. (*) = p<0.05, (**) = p<0.01, (***) = p<0.001, (****) = p<0.0001 v/s PVC group.

Plastic	Contact Angle Water (º)	Young's Modulus (MPa)	Roughness (nm)
PVC	102.2±0.6	25.8±0.7	4.3±1.9
PVC-Ox	70.9±9.3 (**)	NA	NA
PVC-Rf 0%	66.2±12.3 (**)	32.4±0.1 (****)	9.3±2.2 (*)
PVC-Rf 0.1 %	74.4±4.9 (**)	30.5±0.4 (***)	12.1±3.9 (*)
PVC-Rf 1% (24h)	69.2±4.2 (**)	31.3±0.5 (***)	12.9±2.7 (*)
PVC-Rf 1% (48h)	72.1±3.2 (**)	31.2±0.2 (***)	23.1±4.2 (**)

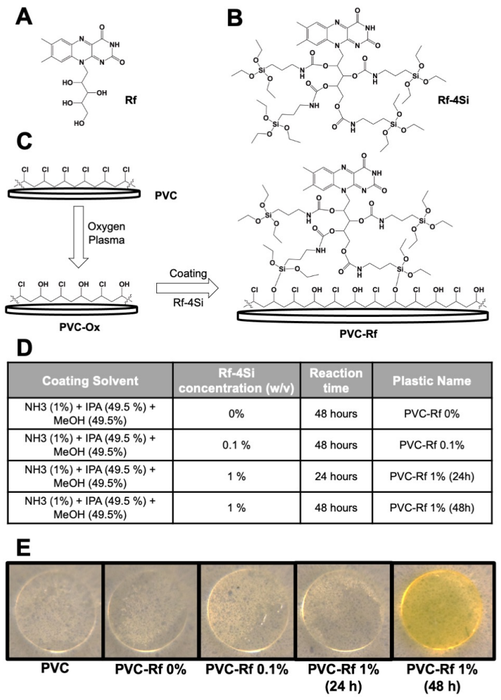

Figure 1. Riboflavin coating scheme, conditions, and representative images. (A) Riboflavin Molecule (Rf). (B) Riboflavin-4 Sililated (Rf-4Si). (C) Schematic representation for the coating process of PVC with Rf-4Si. (D) Summary of the different conditions evaluated. (E) Representative images of the different plastics after treatment. The circular disc diameters were 6 mm in all cases.

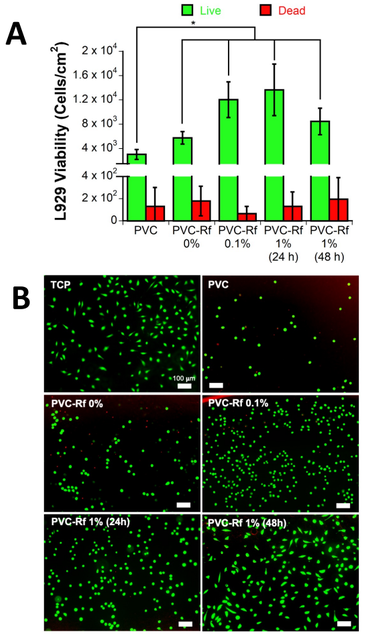

Figure 2. Cell compatibility with the treated plastic. (A) Live/Dead L929 cells viability per cm² for the different groups measured after 24 hours of incubation (n=3). * Denotes p<0.05 calculated from t-test. (B) Representative fluorescence microscopy images of the live/dead assay in the different plastic conditions (TCP = Tissue Culture Plate). Values = mean ± SD.

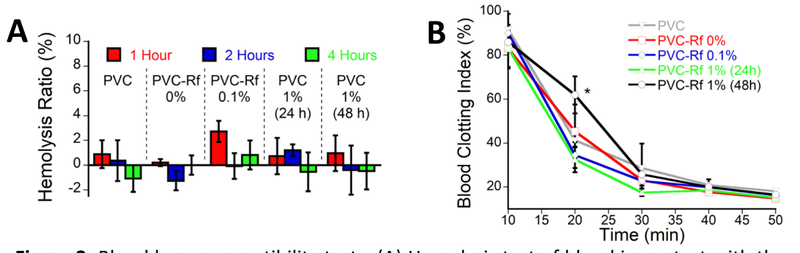

Figure 3. Blood hemocompatibility tests. (A) Hemolysis test of blood in contact with the treated plastics after different incubation times. Values are relative to PBS (0%) and Milli-Q water (100%) without any PVC plastic in both control groups. n=3. (B) Dynamic blood coagulation testing in contact with the treated plastics. The Induced Coagulation Progress (ICP) is a proportional relation index to chemically induced coagulated blood, where 0% = non-coagulated, 100% = fully coagulated. Values = mean ± SD. (*) Denotes p<0.05 calculated from t-test (n=3).

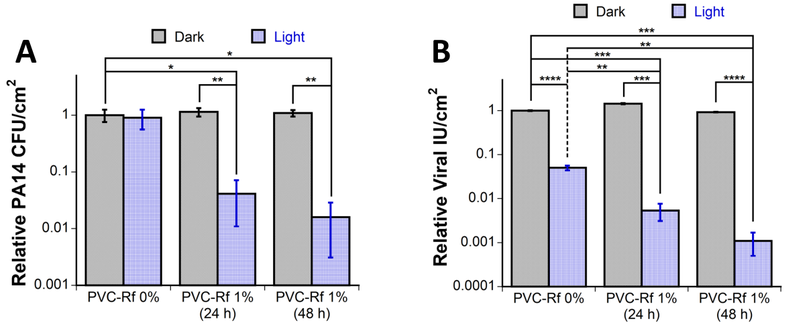

Figure 4. Antimicrobial photoinactivation. (A) Treated plastics in the presence of a biofilm-forming strain PA14. Irradiation was performed with blue light (irradiance of 5.4 mW/cm², for a total dose of 58.3 J/cm²). (B) Viral photoinactivation in the presence of different PVC conditions. A lentivirus model, a surrogate of SARS-CoV-2, was used. Irradiation was performed with blue light (irradiance of 5.4 mW/cm², for a total dose of 29.2 J/cm²). p<0.05 (*), p<0.01 (**), p<0.001 (***), p<0.0001 (****), calculated from the t-test. Values = mean ± SD.

Conclusions

In summary, we developed a simple strategy for surface modification of PVC using a non-toxic riboflavin derivative molecule. The resulting surface modifications improved cell adhesion with no evidence of toxicity, improved human blood compatibility, and reduced clotting. Further, the architectural design of our materials combined with the intrinsic light-activated properties of riboflavin, allowed for blue light-triggered eradication for preformed biofilms of Pseudomonas aeruginosa and lentivirus. Beyond the chemical surface modification of PVC using riboflavin, our approach opens new venues for developing PVC modified surfaces with different dyes with longer absorption wavelengths for light-activated decontamination or with sensing capabilities, both highly sought properties in biomedical devices.