ComfortCoat® Dual-Action Vascular (DAV) Coating

Hemocompatibility

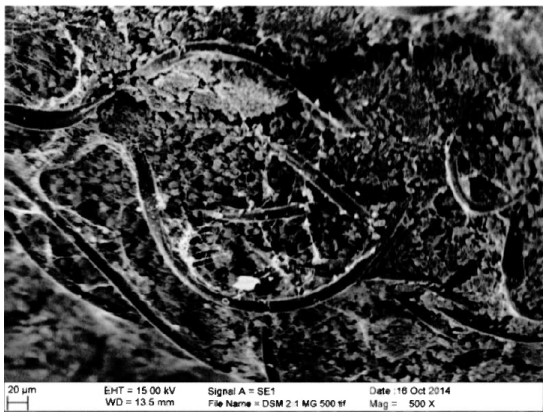
Hemocompatibility is critical for a hydrophilic coating on blood-contacting devices.

By providing hydrophilic coatings to our customers, dsm-firmenich's ComfortCoat® Dual-Action Vascular (DAV) coating can minimize adverse reactions such as thrombosis, hemolysis, inflammation response, and/or activation of blood components (platelets, and the complement system). dsm-firmenich ComfortCoat® coating has undergone extensive hemocompatibility testing. A partnership was started between dsm-firmenich and the University of Tübingen to execute this testing using an in-vitro Chandler loop model. This extensive study included 6 different coating groups on polyamide tubing. These coated tubes were then evaluated per ISO 10993-4 for hemocompatibility testing categories such as thrombogenicity, coagulation, platelets, hematology, and complement system. Each of these evaluations and results are described below [1].

Thrombogenicity

Thrombogenicity is defined as the tendency of a material to promote the formation of a thrombus when it comes in contact with blood.[2] This promotion of thrombus formation is typically observed via SEM imaging to visualize the thrombus on the substrate. In this evaluation ComfortCoat® coated devices performed very well with visibly less thrombus observed on the coated surface compared to an uncoated surface (figure 1).

A.



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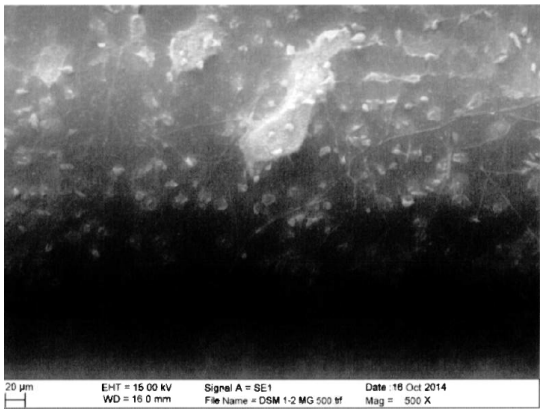


C.

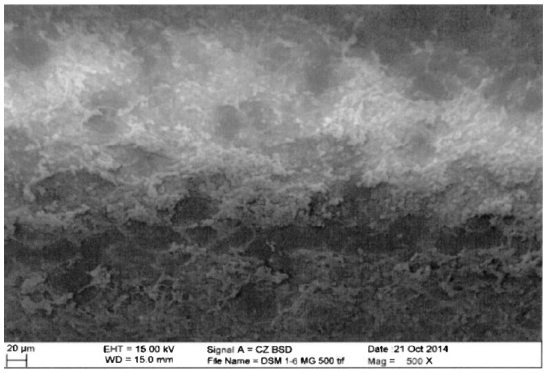


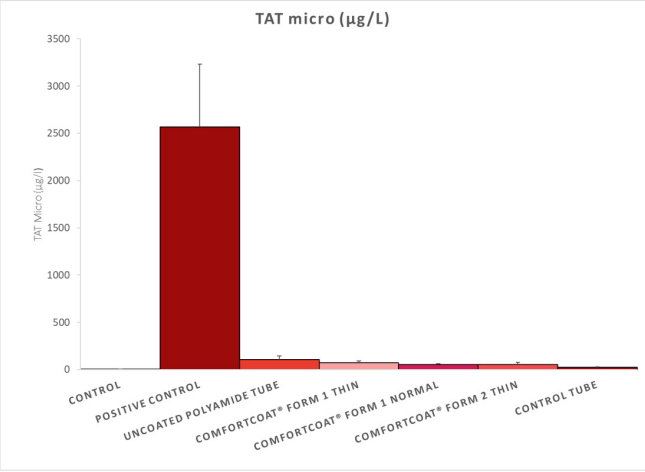
Figure 1: SEM Imaging of **A.** Polyester VG (Control) **B.** Uncoated Polyamide Tube **C.** Polyamide Tube with ComfortCoat® demonstrating visually less thrombus formation when ComfortCoat® is used. Scale: 20µm.

1. All data references have been documented at dsm-firmenich under TD-00590 and associated annexes (TD-00580, TD-00591, TD-00746, TD-00748). Data on file with DSM-firmenich.
2. Ghasemi-Mobarakeh, L., Kolahreez, D., Ramakrishna, S., & Williams, D. (2019). Key terminology in biomaterials and biocompatibility. Current Opinion in Biomedical Engineering, 10, 45–50. https://doi.org/10.1016/j.cobme.2019.02.004

Coagulation

Coagulation is defined as "the action or process of a liquid, especially blood, changing to a solid or semi-solid state" [3]. Coagulation activity can be measured for blood contacting materials by using a Chandler loop model and measuring the thrombin antithrombin-III complex also known as TAT Complex. The TAT complex is a protein complex of thrombin and antithrombin. Blood material contact initiates intrinsic coagulation factors which then generates thrombin. This thrombin is deactivated by complexing with antithrombin forming the TAT complex. Measurement of this complex is a good marker for the detection of coagulation activity. Samples coated withdsm-firmenich ComfortCoat®coating demonstrated low TAT concentrations after blood contact (figure 2) indicating low coagulation activity.

Figure 2: TAT Complex for dsm-firmenich ComfortCoat® and Control Samples- dsm-firmenich has demonstrated low TAT complex compared to the positive control indicating low coagulation activity.



Platelets

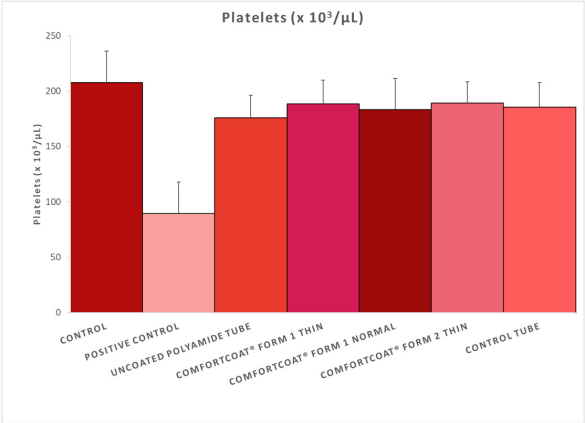
Per ISO 10993-4 platelet assessments were completed by counting the number of platelets in the blood after exposure to ComfortCoat® coated materials, as well as determination of the β-Thromboglobulin (β -TG) concentration.

When blood contacts an artificial surface, this leads to activation and alteration of the platelets. This alteration also leads to loss of platelet functionality. The level of alteration of the platelets can be measured via blood cell counting. After exposure, no strong drop was observed for platelet count in any of the dsm-firmenich ComfortCoat® coated materials when compared to the controls (figure 3a). It is important to note that there is a insignificant drop which is accounted for by platelets sticking to the surface and not destruction.

Platelet activation is a physiological process that occurs when blood vessel walls are damaged and is a pivotal event in hemostasis and thrombosis. When platelets are activated, they release β -TG, and therefore this protein can be used as a marker of this activation (figure 3b). All samples coated with dsm-firmenich ComfortCoat® coating also demonstrated low β -TG compared to the control. Information for both platelet counts and measurement of β -TG indicate that substrates coated with ComfortCoat® have low platelet activation.

Figure 3: 3a Results of Platelet Cell Counting for ComfortCoat® treated materials compared to controls, 3b. β -TG analysis for polyamide tubes coated with ComfortCoat® compared to controls.

A.



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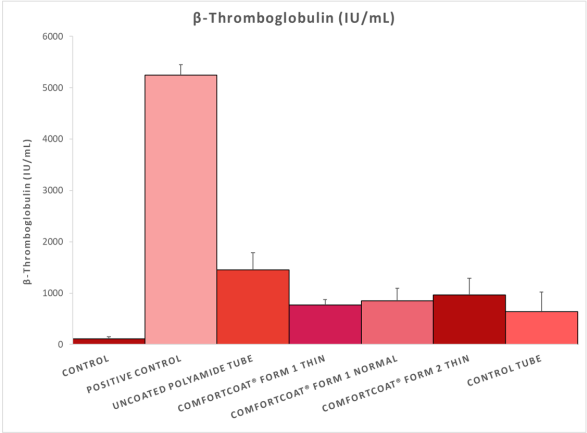
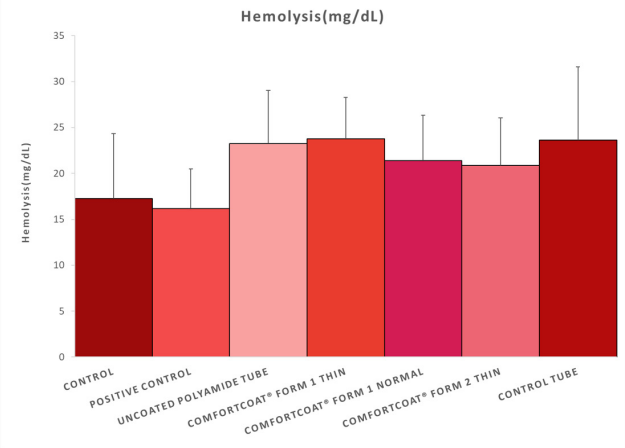


3. Favaloro, E. J., Pasalic, L., & Lippi, G. (2022). Getting smart with coagulation. Journal of Thrombosis and Haemostasis, 20(7), 1519–1522. https://doi.org/10.1111/jth.15691

Hemolysis

Hemolysis is the process of red blood cells breaking down and releasing their contents into the surrounding fluids. When hemolysis occurs it can lead to several other complications such as thrombosis, inflamation, organ damage, kidney disease among others. Hemolysis can be measured via free blood hemoglobin since when hemolysis occurs hemoglobin is released from the cells. Free plasma hemoglobin was within the normal range for all samples coated with ComfortCoat® DAV coating (figure 4).

Figure 4: Hemolysis measured as free blood hemoglobin for ComfortCoat® coated devices compared to controls.



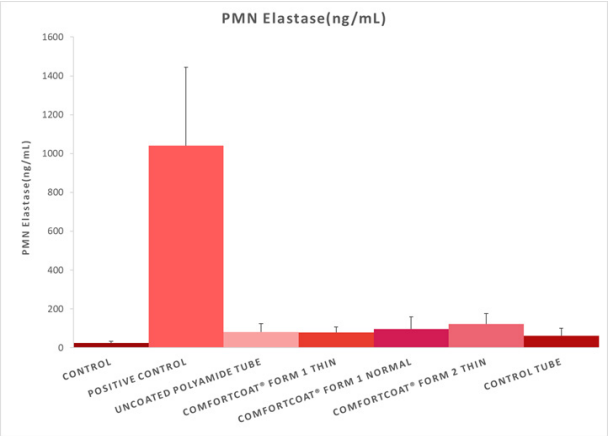
Inflammation

PMN elastase is a proteinase that is used by the granulocytes. This enzyme is released when the neutrophils are activated. Neutrophils are the primary defense cells which respond to pathogens and damaged tissue. When tissue is damaged, or hemolysis occurs, PMN elastase can increase as part of the body's inflammatory response. No significant increase in PMN-Elastase was observed in any of the ComfortCoat® coated samples tested (figure 5).

Complement System Activation

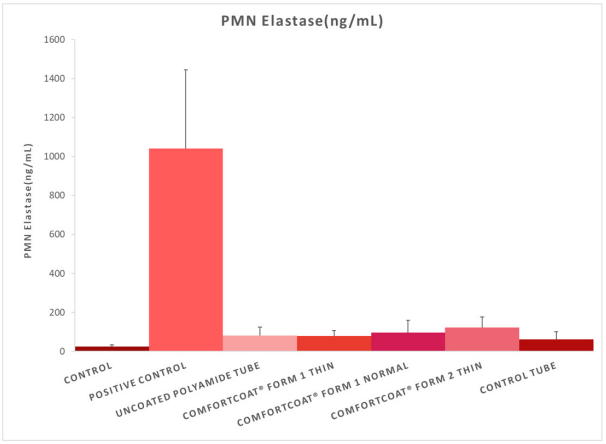
The complement system is part of the immune system and helps the body fight off pathogens and/or damaged cells. Complement activation during blood-material contact takes place as a defense reaction against the supposed pathological invader[4]. When the complement system is activated it produces SC5b-9, a water-soluble protein complex. This SC5b-9, a water-soluble protein complex

Figure 5: Analysis in PMN Elastase in Blood samples after exposer to dsm-firmenich ComfortCoat® coated devices showing no increase in PMN elastase for coated samples vs. controls.



complex can be measured to determine complement activation. Low SC5b-9 indicates low activation of the complement system which was demonstrated by all dsm-firmenich ComfortCoat® test groups (figure 6).

Figure 6: Analysis in PMN Elastase in Blood samples after exposer to dsm-firmenich ComfortCoat® coated devices showing no increase in PMN elastase for coated samples vs. controls.



As shown above, the hemocompatibility of an artificial material can be demonstrated in many ways and can become very complex. The above data was generated in partnership with the University of Tübingen to test polyamide tubes coated with 4 different hydrophilic coating systems. All ComfortCoat® coated groups tested have been proven to demonstrate excellent hemocompatibility properties.

4. Cleveland Clinic medical (Ed.). (2024, May 1). Complement system function. Cleveland Clinic. https://my.clevelandclinic.org/health/body/23370-complement-system