OPTIMIZATION OF DANAPAROID INCORPORATION TO DIALYSIS MEMBRANES FOR LONG TERM HEMOCOMPATIBILITY

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Introduction

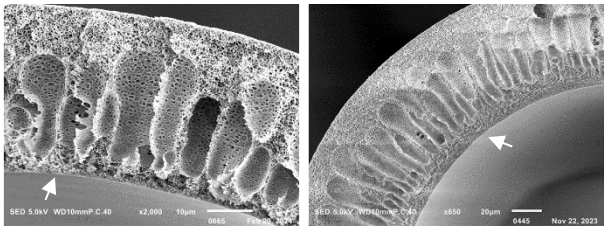
Hemodialysis is one of the main life-saving therapy for patients with end stage renal disease (ESRD) until an organ transplantation becomes available. Currently, ESRD patients undergo non-continuous dialysis therapies (usually for 4 hours, 3 times per week) mainly due to practical, logistical and health-related reasons[1][2]. This leads to a limited toxin removal efficiency because uremic toxins keep accumulating in blood between each dialysis treatments. To enhance patient outcomes and improve their quality of life, more continuous therapies like home or portable hemodialysis are needed, which require membranes with long-term hemocompatibility. Besides, despite advancements in biocompatible materials and membranes, systemic anticoagulation is still required, creating challenges for patients who cannot tolerate anticoagulant administration. Our approach consists in incorporating Glycosaminoglycans (GAGs) to hollow fiber membranes to improve their hemocompatibility. GAGs are long linear polysaccharides that can be found in human's kidney glomerulus, providing natural anticoagulating properties. Our group has recently performed first studies of incorporating various GAGs into hollow fiber membranes, showing that Danaparoid (DP), which is a mixture of different GAGs, can provide improved blood compatibility of polymeric membranes compared to other types of GAGs[3]. In this study we investigated the optimal strategies to incorporate DP to hollow fiber membranes. Ideally, DP should be concentrated in the layer of the membrane that comes into contact with blood and does not leak from this location during therapy.

Methods

We investigated two different strategies to incorporate GAGs: blending in polymer solution and post-treatment coatings. Polymer dope for membrane fabrication consists of polyethersulfone (PES; 16 - 20%), polyvinylpyrrolidone (PVP; 2%) and N-methyl-2-pyrrolidone (NMP; 75 – 79%). DP is dissolved in water at various concentrations and added to the polymer solution. The hollow fiber membranes fabrication conditions are tuned to produce fibers with a small diameter and good mechanical properties. The hollow fiber membranes are fabricated using a conventional spinning setup. Coatings of GAGs is performed with a post-treatment approach.

Results

Figure 1 shows SEM images of two hollow fiber membranes that we fabricated with blended GAGs at different concentrations. Membrane 1 has a higher ultrafiltration coefficient (K_{UF}) due to the lower concentration of DP, which result in a thinner and less compacted selective layer (SL, highlighted by the white arrows). By staining the GAGs within the fibers, we detected the presence of them mainly on the SL of the hollow fiber membranes. To assess the effects of GAGs coating to hollow fiber membranes, we performed preliminary tests of coatings with commercial dialysis membranes. Clean water flux results indicate that the coatings need to be tuned to avoid significant decrease of the K_{UF}.



Membrane 1 – $K_{UF} = 40 \pm 13$ Danaparoid: 30 mg/mL

Membrane 2 – $K_{UF} = 9 \pm 2$ Danaparoid: 60 mg/mL

Figure 1: SEM images of hollow fiber membranes and Ultrafiltration coefficient (K_{UF}).

Discussion

We found that blending is the simplest way to incorporate GAGs to hollow fiber membranes. However, more investigation on the spinning parameters and on the drying process of the fibers are necessary to improve the mechanical properties and permeability of the membranes.

References

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