FROM LAB TO LARGE SCALE: MIXED MATRIX MEMBRANES FOR PROTEIN-BOUND UREMIC TOXIN REMOVAL

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Introduction

Hemodialysis is nowadays the most used therapy for treating End-Stage Renal Disease (ESRD) patients, due to the low availability of transplant organs, which are the best option [1]. However, this treatment presents some drawbacks, it is non-continuous (3 times a week for 4 hours each session) [1,2]. Moreover, commercial filters show a poor capability on removing Protein-Bound Uremic Toxins (PBUTs) such as Indoxyl sulfate (IS) and Hippuric acid (HA). This results in an accumulation of these toxins which is associated to the high mortality rate of ESRD patients [3]. To achieve a better removal of PBUTs, a different type of dialyzer should be used. Our previous studies showed that the application so called Mixed Matrix Membranes (MMM) which combines filtration and adsorption [4] can provide improved the removal of these toxins]. This study highlights the production and testing of MMM with human plasma and full human blood and the route to upscaling their production. The latter could enhance the application of these MMMs into clinical practice.

Methods

Different polymer ratios of membrane forming polymers Polyethersulfone (PES) / Polyvinylpirrolidone(PVP) and spinning settings were used.

Layer	PVP wt%	PES wt%	NMP wt%	ACP wt%
Inner	5	17	78	-
Outer	1,4	14	84,6	*60

*Table 1: Polymer ratios of MMM dope solutions. *60 wt% of the polymer weight. For 10g of PES and PVP, 6g of ACP were added.*

The dual layer MMM was fabricated by extruding polymer dope solutions (PVP / PES) – particle free and particle based – through a spinneret into a coagulation bath with a non-solvent (water). There, the fibers solidify by immersion precipitation and washed for 3 days to remove the solvent (NMP). Afterwards, the fibers are stretched and dried at room temperature.

Laboratory scale mini dialyzers were used to test the PBUTs removal capacity of MMM compared to fibers of commercial dialyzers.

Results and Discussion

Figure 1 presents SEM images of the cross-section of the MMM showing the dual-layered structure and the presence of AC. They have ultrafiltration coefficient (Kuf) of 23 ± 5 mL/(m^2·h·mmHg), within the range of high-flux commercial filters, such as Fresenius FX1000. However, their inner diameter is almost 100% larger.

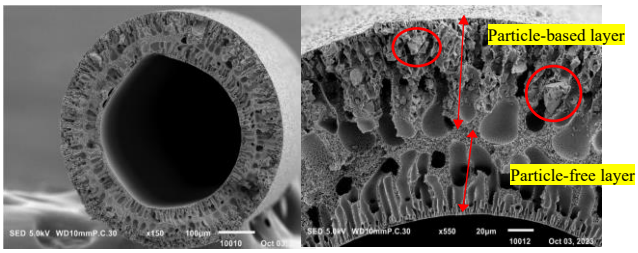

Figure 1: SEM images of the produced MMM. Left magnification x150, Right: magnification x550

Table 2 compares the PBUT removal of the MMM to FX1000. The removal by the MMM was mainly due to adsorption.

	Fibers used	IS [mg·m^{-2}]	HA [mg·m^{-2}]
Human Plasma	FX1000	377 ± 91[4]	2674 ± 564[4]
	MMM	500 ± 176[4]	2478 ± 361[4]
Full human blood	FX1000		
	MMM	1471 ± 364	3060 ± 480

Table 2:PBUTs removal from human plasma and full human blood comparison between MMM and FX1000 in-house laboratory-scale filters.

References

1. Stamatialis, Dimitrios, ed. Biomedical membranes and (bio) artificial organs. Vol. 2. World Scientific, 2017
2. Ter Beek, Odyl, et al. Separation and Purification Technology 225 (2019): 60-73
3. Pavlenko, Denys, et al. Scientific reports (2016)
4. Kim, DooLi, et al. Journal of Membrane Science 609 (2020)

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