DIALYZER MEMBRANES: CURRENT TECHNOLOGY & ADVANCEMENTS

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THE EVOLUTION OF DIALYZER CLASSIFICATION

In this section we will take a look at how dialyzer classification has evolved and how current advances in membrane technology brought about these changes in classification. Also, with these newer membranes, what are some relevant parameters that influenced characterization of membranes.

CURRENT TECHNOLOGY AND INNOVATION IN DIALYZER MEMBRANES

In this section, we will highlight current technology and recent innovations among dialyzer membranes including high cut-off (HCO) and medium cut-off (MCO) membranes, membranes used in newer forms of dialysis modalities such as expanded hemodialysis (HDx) and convective therapies. We will also look at important properties of dialyzers such as hydrophilicity, biocompatibility and endotoxin membrane retention and focus of current membrane research such as bioartificial kidney and mixed matrix membranes (MMM).

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THE EVOLUTION OF DIALYZER CLASSIFICATION

Dialysis membranes are a vital component of hemodialysis, an extracorporeal process in which the blood is cleansed via removal of uremic retention products. Previously, dialysis membranes were classified on the basis of their composition (cellulosic or noncellulosic) or water permeability (low flux or high flux). [1] "Current advances in material technology and chemistry led to the development of membranes with specific characteristics and refined properties. Therefore, additional parameters should now be considered as relevant and these include new permeability indices, the hydrophilic or hydrophobic nature of membranes, adsorption capacity and electrical potential," commented Professor Laurent Juillard, on his session in the World Congress of Nephrology 2022 titled, Innovations in Membrane Technology.

CURRENT TECHNOLOGY AND INNOVATION IN DIALYZER MEMBRANES

Advancements in dialyzer membranes enabled clasification of membranes based on water permeability, middle molecular weight and albumin depuration. Medium cut-off (MCO) and high cut-off (HCO) membranes are compared in Table 1.

	Characteristics	Clinical use	Others
High cut-off (HCO) membranes	High-flux and protein leaking with β2 microglobulin sieving coefficient of 1.0	Myeloma-associated acute kidney injury, continuous kidney replacement therapy (removal of inflammatory mediators)	High albumin loss precludes long-term use for ESKD patients
Medium cut-off (MCO) membranes	Steep sieving curve (increased removal of β2 microglobulin and decreased albumin loss)	Hemodialysis treatments, with removal of an expanded range of uremic toxins vs. conventional high-flux membranes*	Represents the basis for expanded hemodialysis

Table 1. Characteristics and clinical uses of high cut-off (HCO) and medium cut-off (MCO) membranes. Adapted from Ronco C, Clark W, Nat Rev Nephrol 2018;14(6):394-410 and *Boschetti-de-Fierro A, et al, Sci Rep 2015; 5: 18448. [2]

Moreover, new membranes enabled the development of new dialysis therapies. The development of high-flux membranes paved the way to the use of convective therapies such as hemodiafiltration (HDF) and medium cut-off (MCO) membranes for expanded hemodialysis (HDx). The benefit of reducing mortality outcomes was linked to high convection volumes (>23 L/session) and resulted to a 22–31% reduction in mortality risk based on an individual pooled analysis of data from four large RCTs on HDF. [3,4] Other important features of new membranes include improved hydrophobic-hydrophilic balance by the addition of compounds such as polyvinylpyrrolidone (PVP) to synthetic membranes and addition of hydroxyl and vitamin E on cellulosic membranes to improve biocompatibility. [5,6]

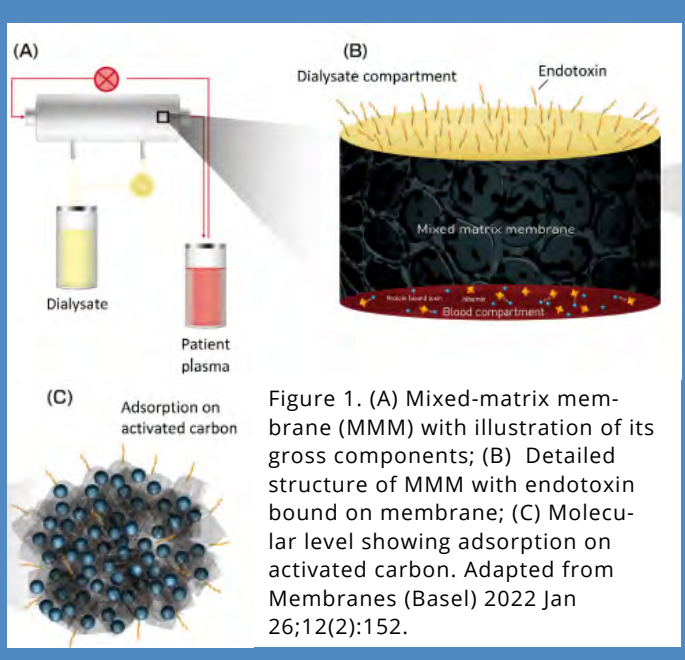

Figure 1. (A) Mixed-matrix membrane (MMM) with illustration of its gross components; (B) Detailed structure of MMM with endotoxin bound on membrane; (C) Molecular level showing adsorption on activated carbon. Adapted from Membranes (Basel) 2022 Jan 26;12(2):152.

Membranes with high endotoxin retention help prevent inflammation from dialysate contamination from endotoxins which are by-products of bacterial processes. [5] Further development of membrane technology focuses on research centering on next generation membranes such as bioartificial kidneys that mimic native kidney via a monolayer of immortalized proximal tubule epithelial cells (ciPTECs) cultured on membranes and collagen. Another example is the mixed matrix membrane (MMM) with its improved blood purification characteristics through combination of filtration and adsorption mechanisms. [6] (Figure 1)

EXPERT COMMENTARY (With Dr. Bernard Canaud)

A few years or maybe a decade down the line, how do you foresee the direction of development of membranes toward better patient outcomes?

"Dialysis membrane remains as a crucial component of the hemodialysis system to optimize solute removal efficacy and to minimize blood membrane biological reactions. They are parts of a treatment chain that should be operated in optimized conditions and adjusted to patient needs and tolerance, in order to improve patient outcomes. There are significant improvements made over the years but further progresses are required to bridge the gap of native and artificial kidney functions.

From my perspective, innovative and future development of membrane technology will have to address three main concerns: Firstly, to minimize dialyzer size and improve hemocompatibility to permit development of a wearable or totally implantable bioartificial kidney. In this perspective, silicon nanopore membranes (SNM) may facilitate such medical device development. Secondly, heparin-free dialysis remains a holy grail for extracorporeal treatment. Research is progressing relatively fast in this field. The incorporation within the core polymer (membrane and tubing) or grafting onto the surface of an antithrombotic agent has shown some encouraging results. Thirdly, protein-bound uremic toxins (PBUTs) (i.e., p-cresyl sulfate and indoxyl sulfate) remain poorly removed by conventional dialysis including hemodiafiltration. This limitation is due to their high degree of albumin binding (>90%) and poor clearance of free fraction. Several approaches are currently explored including use of albumin leaking membrane, ionic unbounding capacity resulting from infusion of high ionic strength solution or the continuous infusion of competitor displacers (e.g., Ibuprofen). Adding an adsorber on extracorporeal circuit or developing a multilayer membrane including sieving and adsorbing capacities offer interesting perspective since they would have the capacity to clear more efficiently PBUTs. Now, from a kinetic perspective, it seems that the most effective option to ensure significant PBUT removal would be to combine the infusion of a competitive displacer with an adsorptive system (multilayer membrane) to increase clearance of PBUTs by optimizing bound to free fraction gradient."

Dr Canaud suggested a published review article for further reading on the advances of dialysis membranes. [7]

References:
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