MCO Membranes: Enhanced Selectivity in High-Flux Class

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BACKGROUND

One of the unmet needs in hemodialysis is the adequate removal of uremic toxins over a broad molecular weight range. As synthetic membranes are less selective than the glomerular membrane, current hemodialysis membranes do not remove higher molecular weight toxins appropriately. Consequently, patients on hemodialysis have higher levels of middle and large molecular solutes in plasma.

Membrane innovation is currently directed towards enhanced removal of uremic toxins and increased membrane permeability. During the last decade, some experience has been gathered with high permeability membranes such as high cut-off (HCO) membranes. Pilot trials with HCO membranes indicated that expanded toxin removal might benefit the patient by decreasing the general inflammatory state.

Medium cut-off membranes were designed to deliver expanded toxin removal as observed with **HCO** membranes while retaining albumin (65 kDa)[1] so that they are appropriate for regular use in conventional treatment schedules and treatment mode (i.e. 4-hour treatments, three times weekly in Europe).

OBJECTIVE

The aim of this study was to present the characterization of four prototypes of novel **MCO** membranes by dextran filtration[¥]. In addition, the sieving properties of the membranes before and after blood contact were reported, and the pore size during operation (i.e. hemodialysis treatment) was compared to the size of uremic toxins and vital proteins.

[¥]Fractional clearance studies to measure the size selectivity associated with glomerular filtration have universally employed dextran as a test transport probe. It is neither secreted nor reabsorbed by the renal tubules, so its clearance is easily measured.[2]

METHODOLOGY

Four different types of prototype devices denoted as **MCO** membrane 1 to **MCO** membrane 4, which differ in permeability, were investigated. As reference, a HCO device (**Theralite** dialyzer) and a conventional high flux membrane (**Revaclear** dialyzer) were also tested. All devices were manufactured by Gambro Dialysatoren GmbH, Hechingen, Germany. The membrane material was a polyarylethersulfone/polyvinylpyrrolidone blend.

Membranes were characterized in minimodules with the same surface area, nominal length, inner diameter and wall thickness. The minimodules were immersed in water before the filtration experiments. Minimodules intended for characterization after contact with blood for simulating in vivo operation conditions were initially perfused with blood (bovine) for 40 minutes and rinsed afterwards with water.

Dextran solutions were prepared, and filtration experiments were carried out. For experiments run on **MCO** membrane 4, the dextran solution included one additional fraction of 150 kDa, to allow for sieving coefficient (SC) calculation with similar precision as the other **MCO** membranes.

RESULTS

Characterization of the **MCO** high-flux membranes by dextran sieving profiles in aqueous solution (pristine; before blood exposure).

As shown in Figure 1, the sieving curves for the **MCO** membranes are located at the molecular weights between that of the conventional high-flux membrane and **HCO** membrane in aqueous solution (pristine; before blood exposure). The **MCO** membrane sieving curves are similar to the ficoll sieving curve for the glomerular membrane; blood purification membranes should mimic the filtration spectrum of the natural (glomerular) membrane.

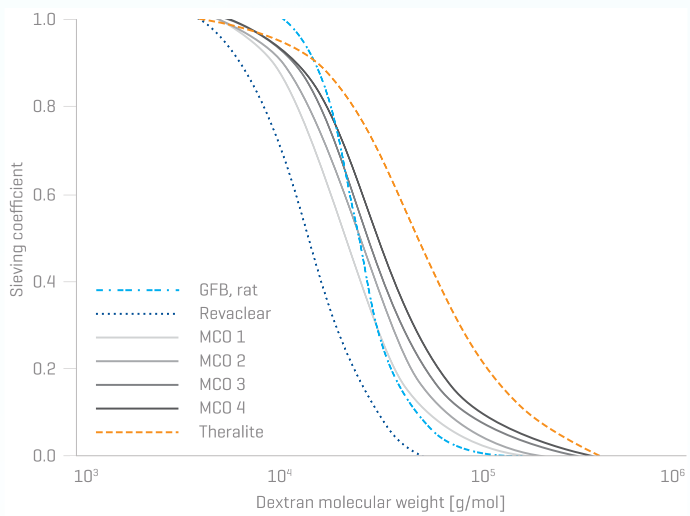

FIGURE 1. Characteristic in vitro dextran sieving curves measured in aqueous solution (pristine/before blood exposure) for different types of blood purification membranes: high-flux (Revaclear, MCO membranes 1-4), HCO (Theralite). Data for glomerural membrane added for comparison (rat specimen, ficoll filtration, measured in vivo).

The values for Medium Weight Retention Onset (MWRO), Medium Weight Cut Off (MWCO) and pore radius (i.e. effective Stokes-Einstein radius calculated from MWCO) are depicted for the four membranes, as well as the conventional high flux membrane and **HCO** membrane in Table 1. The differences between the **MCO** membranes are evident from 1 to 4, showing increased MWRO and MWCO values which indicate increased permeability.