Membrane chromatography cassettes for bind and elute applications of viruses and large proteins

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1. Introduction

For flow-through polishing applications membrane adsorbers have become a well-established technology. However, there is an increasing demand for bind and elute purifications for larger targets as aden- and lentiviruses, virus like particles (VLP) and influenza. The reason is the higher binding capacity of macroporous membranes compared to conventional resins having much smaller pores and excluding them by size.

But capture applications with such devices suffered from the current size limitation of 5 liters e.g. in the Sartobind® Q or S Jumbo 5 L. Here we describe a modular cassette system which has been tested for scale-up and flow performance in comparison with void volume optimized capsules. The goals were to create a system up to 20 L which can be optionally expanded to ~100 L and, for able adapt exactly to the size needed (modular), using the same 4 and 8 mm bed height as the capsules and membranes for single- or intra batch re-use.

2. The cassette design: 2 membrane stacks 4 ± 8 mm

In capsules the membrane is rolled up. To achieve the same flow pattern in the cassette, a cut through a capsule suggests two stacks of membrane with a central inlet flow channel. The fluid enters on top between the stacks and travels through these to the outside (downstream) channels and then to the outlet (Fig. 2d). By this design approach the principal fluid path is maintained.

3. Comparison of capsule and cassette fluid paths

Figure 5 shows the construction of the standard membrane adsorber devices in the 4 and 8 mm void volume optimized design. In the cassette (Fig. 6) the same flow principle is applied as in the existing options as flow-ports perpendicular through the membrane and through void volume optimized fluid channels.

4. Scaleability

The scale-up from existing adsorber capsules to cassettes is essential.

To compare breakthrough performance, devices were loaded with a 2 g/L bovine serum albumin (BSA) solution in 20 mM Tris/HCl pH 7.2. The equilibration was performed using 5 MV of equilibration buffer. The flow rate was 5 MV/min. 1.6 L Cassettes were loaded with 3.3 CV of 2 g/L BSA which was removed. The flow rates were measured using a flow meter (Masterflex L/S, pH 7.2) and a 3.75 CV/min (SC), 0.67 CV/min (Resin A), 1 CV/min (Resin B) flow rate was used.

5. Virus capture on AIXE (Q) and sulfated cellulose (SC) adsorsers vs. resins

Evaluation of the recently developed SC displays 5-7 x higher binding capacity of viruses particles (VPs) and M protein of Ad 5 than the conventional resins.

6. Summary

The Sartobind® Cassette system is a prerequisite for large scale bind & elute membrane chromatography. Combined with anion exchangers and newly developed virus capture membranes such as sulfated cellulose adsorbers it intrinsifies manufacturing of virus and VLP.

7. References