Simplifying Progress

Advances in mAb Purification With Optimized Membrane and a New Screen

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1. Introduction

Tangential flow filtration (TFF) is essential in downstream processing, particularly with the increasing demand for subcutaneously administered monoclonal antibodies (mAbs) that require high final product concentrations. Selecting the right consumable for the final ultrafiltration | diafiltration (UF | DF) step is crucial.

In TFF cassettes, channel geometry is vital for meeting application requirements. A channel that is too narrow may hinder achieving the target concentration due to pressure constraints, while a channel that is too wide can unnecessarily prolong processing time and increase pump-induced shear on the product. Beyond channel geometry, the membrane is key to optimal performance. It must withstand typical cleaning agents like NaOH, ensure complete product retention, and provide high permeability. Although membrane permeability is less influential in high-concentration mAb UF | DF due to gel layer formation, increased permeability enhances pre-process flushing and other non-filtration steps.

This poster shows how different factors influence the performance of the new Sartocon® Q Hydrosart® 30 kDa mAb cassette. First, we focus on the new Hydrosart® 30 kDa ultrafiltration membrane itself, before evaluating the combination of the tailored membrane with the optimized channel design.

2. Investigation on Ultrafiltration Membranes

The new TFF cassettes optimized for mAb applications features a 30 kDa Hydrosart® membrane specifically designed for final UF | DF in mAb processing. In contrast to the standard 30 kDa Hydrosart®, the membrane flux and retention profile of the mAb-optimized membrane is tailored to the needs of of mAb applications. Retention is fully maintained for mAbs, but could be reduced for smaller molecules. At the same time, the permeability for water and buffer solutions is significantly increased. Compared to an equivalent competitor membrane, the measured molecular weight cut-off (MWCO) of the new membrane remains lower, although the water permeability is higher (Figure 1).

Figure 1: *Correlation Between the 90% MWCO (Determined Through Dextran Sieving Curves) and the Membrane Permeability for Arium® Water*

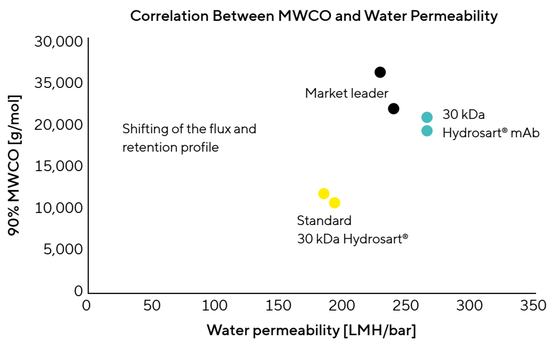
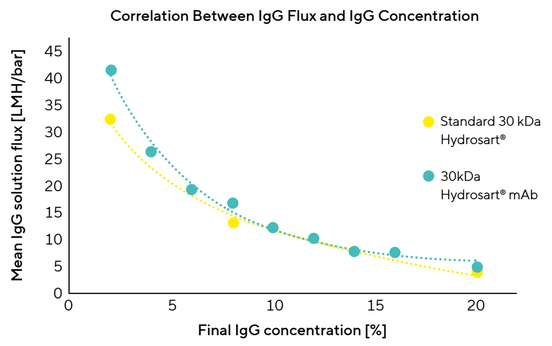
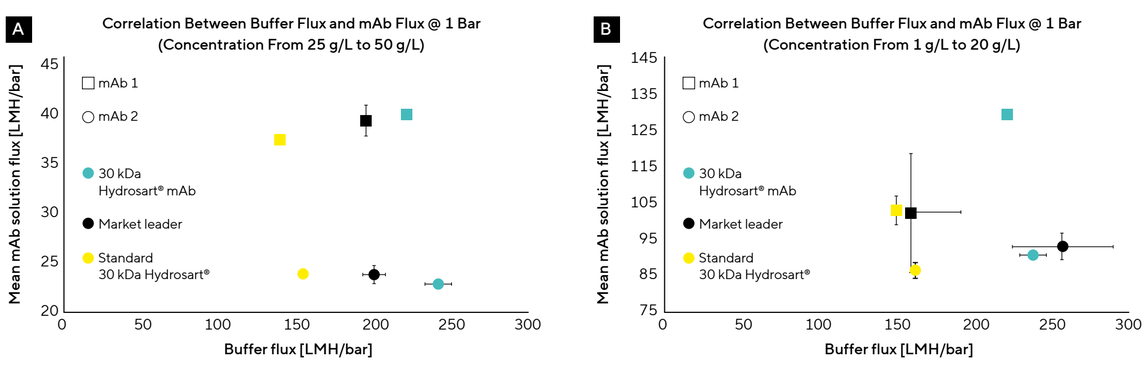


Figure 2: *Mean Flux of IgG Solution Depending on its Concentration (2-Fold Concentration in Amicon® Stirred Cells at 1 bar and 1,100 rpm)*



Filtration runs on the membranes in stirred cell trials with Immunoglobulin G (IgG) and different mAbs showed a potential correlation between water permeability and the mAb solution flux. However, the effect is strongly dependent on both the molecule concentration and the type of molecule (Figures 2 and 3). While the processing time can be significantly improved for one mAb, there might be no significant differences for another mAb.

Figure 3: *Correlation Between Buffer Flux and the Flux for Different mAbs During Stirred Cell Trials at 1 bar and 1,100 rpm When Concentrating From* ***(A)*** *25 g/L to 50 g/L and* ***(B)*** *1 g/L to 20 g/L*



Note. mAb1: histidine buffer, pH 5.5; mAb2: 1x PBS Buffer, pH 7.4

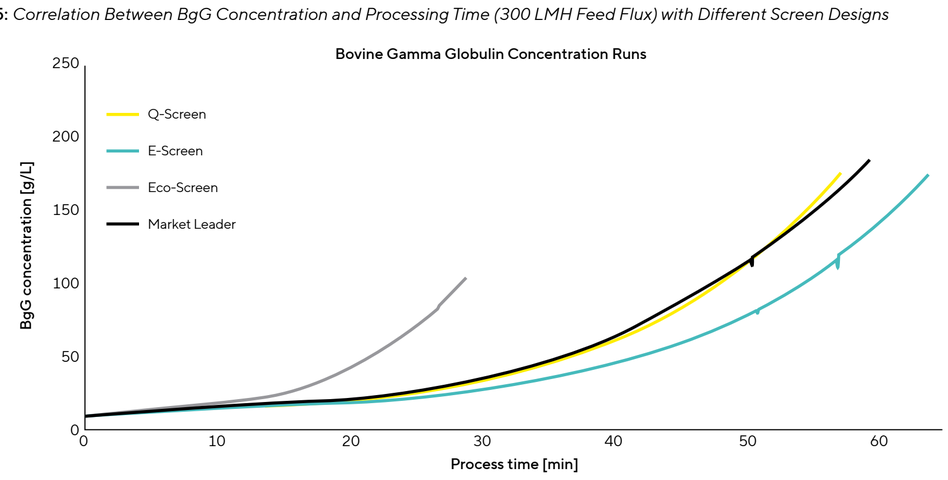
3. Investigation of TFF Cassettes

Figure 4: *Ambr® Crossflow & Sartocon® Q Slice 100*

In order to efficiently conduct TTF trials, the Ambr® Crossflow System was used in combination with the newly designed Sartocon® Q Slice 100 cassette. This combination enables a multi-channel setup with a cassette format that is linearly scalable from an effective filtration area of 86 cm² up to 3 m² in the Sartocube® format, and even beyond, with a consistent flow path length. In addition, all cassette formats are designed without the intentional use of PFAS.

Using this setup, the new Hydrosart® 30 kDa mAb cassette was evaluated together with the existing ECO and E-Screen Hydrosart® cassettes as well as the current market leading product. For this, pure concentration runs were conducted using bovine gamma globulin (BgG) as a model solution (Figure 5).

Figure 5: *Correlation Between BgG Concentration and Processing Time (300 LMH Feed Flux) with Different Screen Designs*



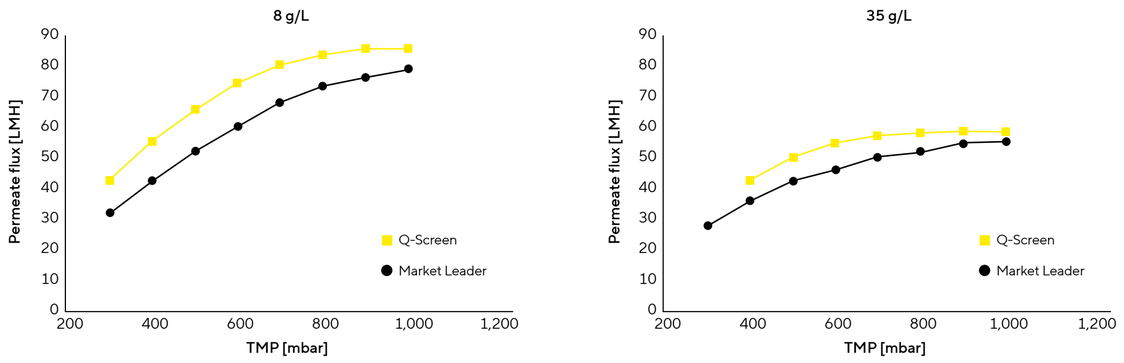
For lower BgG concentrations up to 120 g/L, the ECO screen cassette can process material efficiently at 300 LMH feed flow due to its narrow channel design, but it may reach the inlet pressure limit more quickly at higher target concentrations. In contrast, the E-Screen cassette can handle high viscosities but typically has to be operated at higher feed flow rates to maintain efficiency. The Q-Screen cassette combines the benefits of both channel types, allowing fast processing at medium to high viscosities.

In general, the achievable final concentrations can be significantly increased by reducing the feed flow rate towards the end of the process. With this approach, the Q-Screen cassette processed up to 235 g/L final concentration in a separate trial with an antibody solution.

In a further investigation, characteristic transmembrane pressure (TMP) curves were evaluated using 8 g/L and 35 g/L antibody solutions at a 250 LMH feed flow rate (Figure 6). In comparison to the corresponding competitor product, an increased permeate flux, especially in regions of lower TMPs, was observed.

Processing at lower TMPs is advantageous, as reduced heat generation lowers the risk of temperature increases that hinder processing as well as limiting shear stress to the target mAb.

Figure 6: *TMP Scouting for 8 g/L (Left) and 35 g/L (Right) Antibody Concentrations at 250 LMH Feed Flow*



4. Usability

In addition to protein flux performance during a typical cycle of a reusable TFF cassette, several steps depend on the nominal water permeability (NWP) of the cassette. These steps include the pre-flush before sanitization, the flush between sanitization and equilibration, rinsing immediately after UF | DF (including potential recovery), and the final rinsing after CIP.

Based on rinsing recommendations for all these steps, the overall flushing volume is 300 - 400 L/m², considering a feed-to-retentate ratio of 1:1. This corresponds to a total rinsing volume of 150 - 200 L/m² through the membrane.

With a TMP of 1 bar and a device permeate flux rate of 125 LMH/bar, the total flushing time amounts to approximately 70 - 100 minutes. The new 30 kDa Hydrosart® mAb offers a 50% higher nominal water flux compared to the standard 30 kDa Hydrosart®, resulting in a 30-minute reduction per cycle. Depending on the process, this can save more than 10% of the total process time. Moreover, shorter rinsing times reduce energy consumption and improve equipment utilization, contributing positively to sustainability.

4. Conclusion

The advancements in Sartorius' 30 kDa ultrafiltration membranes and the new Sartocon® Q cassettes demonstrate significant improvements in downstream processing for mAbs With optimized channel geometry and membrane characteristics, they offer enhanced permeability and tailored retention profiles, leading to more efficient processing in mAb applications.

This study shows that Sartocon® Q cassettes can be efficiently operated for medium and high target concentrations while requiring comparatively low TMPs. This reduces heat generation, minimizes temperature-related challenges and limits shear stress.

The setup used for the performance trials, based on Ambr® Crossflow and the new Sartocon® Q Slice 100, provides a convenient solution for screening as well as initial scale-up investigations.

The correlation between water permeability and mAb solution flux, as observed in filtration trials, underscores the importance of molecule-specific considerations in processing. While for some mAb materials there is a correlation between NWP and protein flux, in other cases the membrane has only minor influence, and turbulence promotion in the feed–retentate channel is the main driver of performance.

The new Hydrosart® 30kDa mAb membrane's higher nominal water flux significantly reduces flushing and rinsing times, cutting process time by 10% or more. It also promotes sustainability through lower energy consumption and more efficient equipment use. These advancements position Sartorius' TFF solutions as a pivotal component in meeting the growing demand for high-concentration mAb products, ensuring both performance and sustainability in biopharmaceutical manufacturing.