Application Note

Scalable Process Filtration with Opticap® XL 150, 300 and 600 Capsules with Millipore Express® Membranes

INTRODUCTION

Opticap XL 150, 300 and 600 capsules with Millipore Express membranes provide customers with quick and predictable scale up using relatively small process volumes. This application note evaluates the scalability of these small-scale capsules (SSC) to both autoclavable and gamma three-inch and 10-inch cartridges containing Millipore Express membrane. *Note: Opticap XL3 and XL10 capsules were tested as capsule subassemblies (three-inch and 10-inch cartridges).* Scalability was determined by comparisons of water permeability and capacity with two model streams, soy peptone and Bovine Serum Albumin (BSA), under constant pressure conditions. The two model streams represent high and low fouling process streams. The membrane areas tested were between 13.8 and 6073 cm^2, representing a 440 fold scale up for predicting performance.

OBJECTIVE

Determine if the performance of Opticap XL 150, 300 and 600 capsules with Millipore Express membranes can predict process performance of three-inch and 10-inch devices. Scaling factors are provided to account for discrepancies among the various scales.

METHODS AND MATERIALS

Membranes and Supports

Millipore Express SHC (Sterilizing High Capacity) filters contain an on-board polyethersulfone (PES) membrane prefilter (nominally rated at 0.5 µm) and a sterilizing-grade PES 0.2 µm membrane. The prefilter layer protects the 0.2 µm membrane from premature plugging for extended filtration capacity. Non-woven supports comprised of polypropylene or polyester sandwich the pleated membranes in the device to maximize effective filtration area and aid in protecting membranes from extreme process conditions. The support-membrane configuration also provides fluid flow access between the pleats.

Three-inch and 10-inch Opticap capsules with Millipore Express SHC membranes, noted as SHC-Autoclavable and SHC-Gamma contain specialized support materials. Polyester support in the SHC-G devices provides gamma stability and polypropylene support in SHC-A cartridges delivers autoclave and caustic stability. Different filtration areas result when these specialized support materials of different thickness are pleated with Millipore Express membranes. Effective filtration area (EFA) for each device is listed in Table 1.

Table 1. **Device Filtration Areas**

	Effective Filtration Area							
	Flat Disc	Opticap XL			SHC-A		SHC-G	
Size	47 mm	150	300	600	3-inch	10-inch	3-inch	10-inch
Area (cm^2)	13.8	144	294	586	1696	5339	1929	6073

PROCESS STREAMS

High-fouling media was mixed in 200-800 liters of RO water containing 0.2 g/L Hy-Soy T Peptone and 1 g/L sodium phosphate monobasic, sodium phosphate dibasic, sodium chloride and Pluronic F68 surfactant. A 225 or 1,000 liter pressure vessel was used to deliver high-fouling media.

Low-fouling media was mixed in 600 – 800 liters of RO water containing 50 g/L media grade BSA in 10mM PBS. A 1,000 liter pressure vessel was used to deliver low-fouling media.

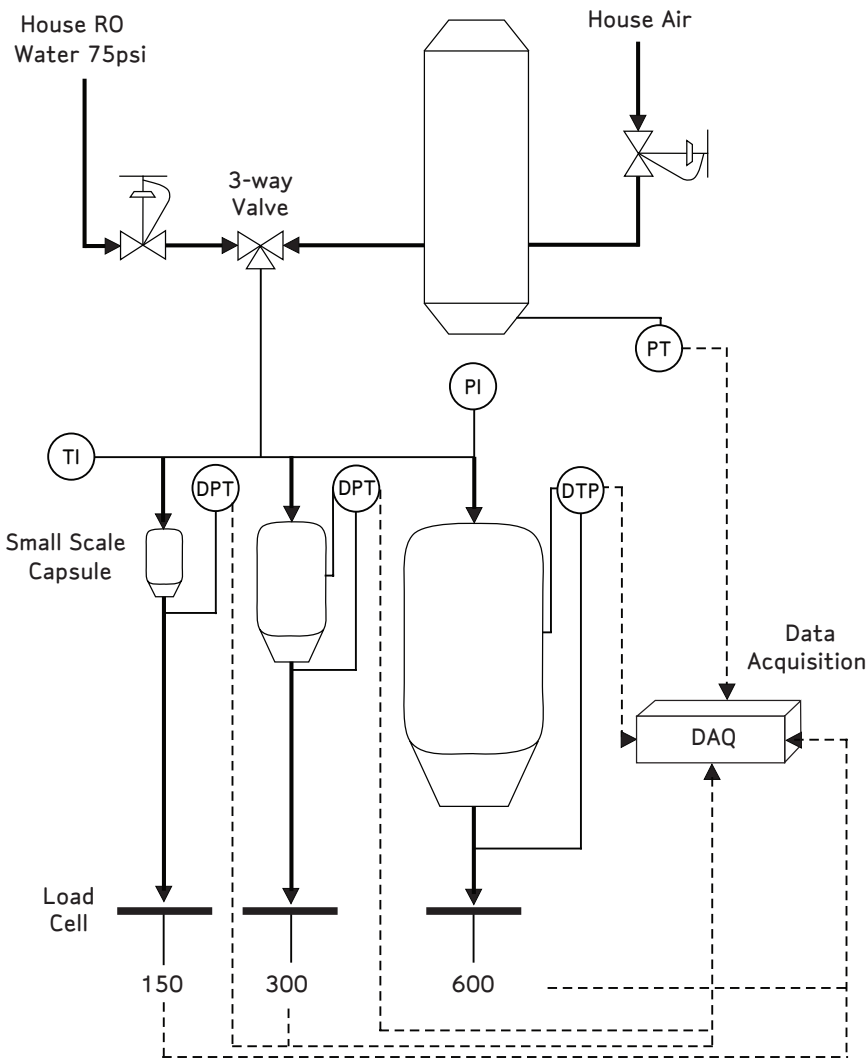
TEST SYSTEMS

Two systems were used for method development and final process testing.

The Opticap XL system (shown in Figure 1) was designed for 0.5 – 50 liters and is capable of monitoring trans-membrane pressure, permeate weight as well as media temperature. A data acquisition system (DAQ) was used to collect pressure data and permeate weight from a maximum of three SSC devices simultaneously. Temperature was recorded manually.

Due to large process volumes (600 – 800 liter) the Opticap capsule with Millipore Express membrane cartridge test stand (shown in Figure 2) required a centrifugal pump to deliver a constant feed pressure. The three-inch and 10-inch SHC cartridges were tested individually and tandem load cells were used for permeate collection.

Figure 1. **Opticap XL Test System**



TEST METHOD

To prevent air entrapment, the upstream water and media lines were thoroughly purged before device installation. A three-way valve provided fluid flow continuity when switching between water permeability and throughput tests.

Wetting

Release the downstream to the atmosphere and open the upstream vent. Devices were wet with clean RO water for two minutes at 5 psi differential pressure (Δ P).

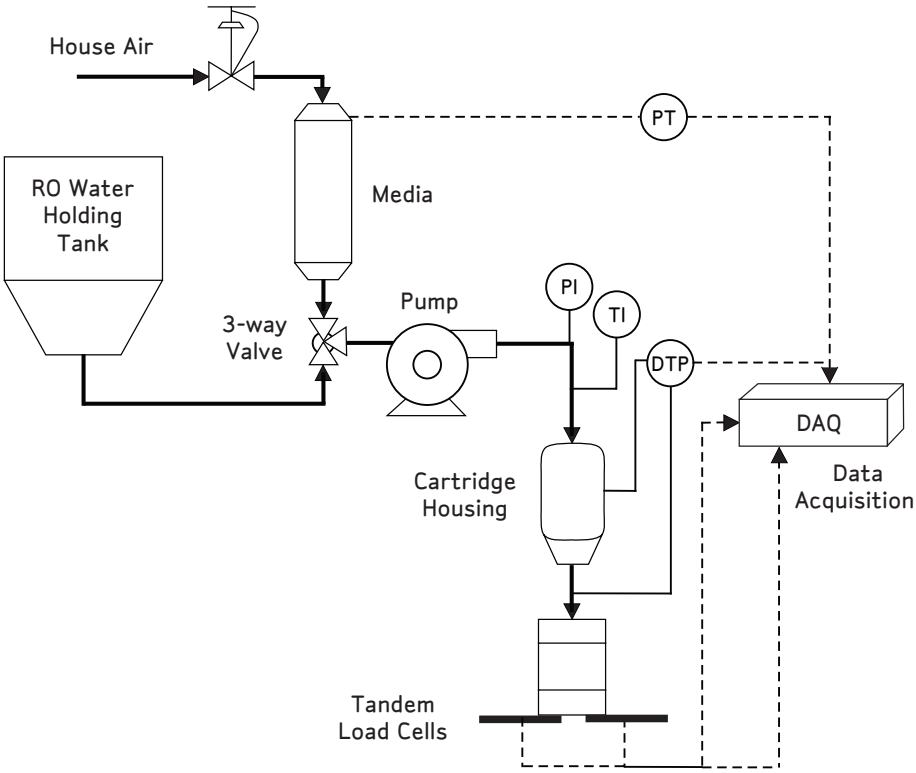
Water permeability

Increase the differential pressure across the filter to 10 psi, vent the upstream side of the filter and collect the permeate for two minutes.

Throughput

Switch the three-way valve to the media and run the media at 10 psid. Collect high-fouling permeate for 20 minutes and low-fouling for 30 minutes. Flush the system thoroughly with water before subsequent runs.

Figure 2. **Opticap Capsule with Millipore Express Membrane Cartridge Test System**



RESULTS

Water Permeability

Water permeability data of the tested devices is summarized in Figure 3. Mean water permeability of all devices was 952 lmh/psi (dashed line). Permeability measured on 47mm discs (n=11) matched the permeability of SHC-A pleated devices. The darker shaded bars represent an alternate membrane lot and these devices were normalized to the three-inch cartridge data from both membrane lots. Permeability of Opticap XL 150, 300 and 600 devices with Millipore Express SHC membranes was ± 18% of values for SHC-A 10-inch devices. Permeability of Express Opticap XL 150, 300 and 600 devices with Millipore Express SHC membranes was ± 8% of values for SHC-G 10-inch devices.

Figure 3. **Water Permeability**

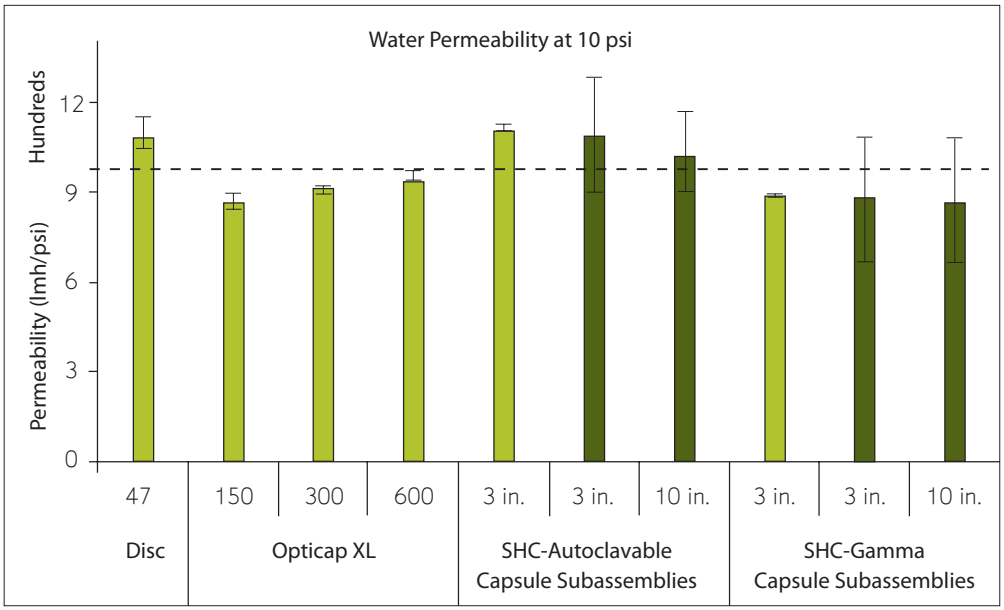
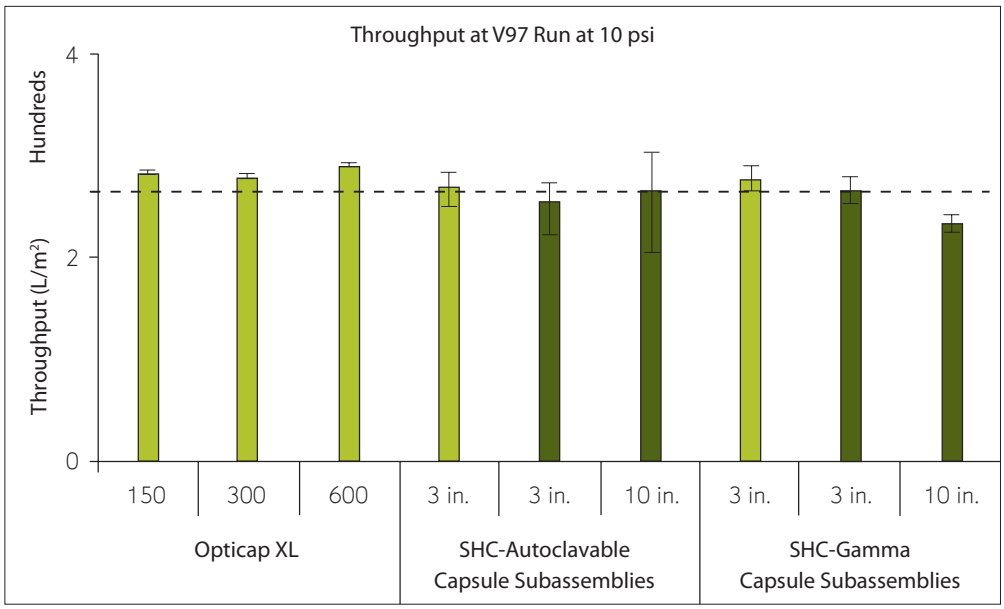


Figure 4. **Device Throughputs for High-fouling Media**



THROUGHPUT

Throughput at 97% flux decay with high-fouling soy stream is summarized in Figure 4.

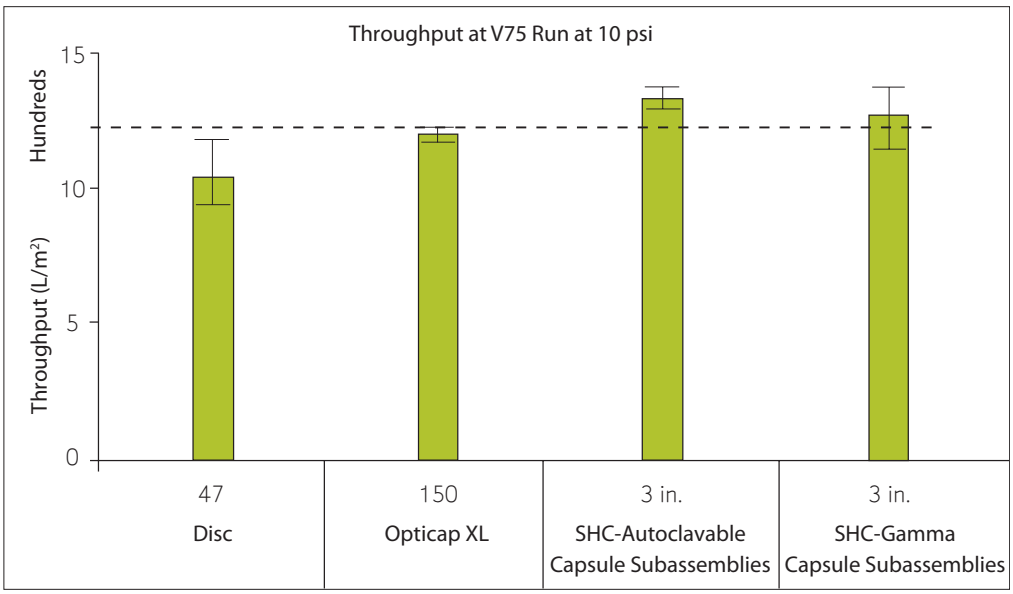
Mean throughput of all devices was 269 L/m^2 (dashed line). The dark shaded bars represent an alternate membrane lot which was normalized to the three-inch cartridge data which is represented by the light shaded bars. Throughputs of Opticap XL 150, 300 and 600 capsules with Millipore Express SHC membrane devices were within ± 9% of SHC-A 10-inch devices and within ± 19% of SHC-G 10-inch devices.

Throughput at about 75% flux decay with low-fouling BSA stream is summarized in Figure 5.

Mean throughput of all devices was 1,287 L/m^2 (dashed line). Throughput (L/m^2) measured on 47mm membrane discs (n=4), tested with membrane from the same membrane lot as the devices, trended lower than the pleated devices. The lower throughput measured on membrane discs vs. pleated devices was attributed to the absence of support material on the upstream side of the membrane which provides some prefiltration benefits to the membrane. This upstream support material is present in pleated devices but is not included with membrane discs.

Throughputs of Opticap XL 150 devices with Millipore Express SHC membranes were within ± 12% of SHC-A three-inch devices and within ± 7% of SHC-G three-inch devices.

Figure 5. Device Throughputs for Low-fouling BSA Media



THROUGHPUT CURVES

Scalability can also be shown as in Figure 6 with the complete plugging profile. The vertical dashed line at 15 minutes denotes 97% flux decay (V97) and also represents the time point of corresponding throughput data in Figure 4.

With high-fouling media, the Opticap XL devices demonstrated similar plugging behavior as the three-inch cartridges for predictable throughput performance.

Figure 7 provides complete plugging profiles similarly for the low-fouling BSA media. The vertical dashed line at 15 minutes denotes 70 – 80% flux decay (V70 – 80) and also represents the time point of corresponding throughput data in Figure 5.

With low-fouling media, the Opticap XL 150 device demonstrated similar plugging behavior as the three-inch cartridges for predictable throughput performance.

Throughput measured on 47 mm discs (see Figure 7) was effected by the absence of specialized support material on the upstream side of the membrane. These membrane discs, which were taken from the same membrane lot as the pleated devices, show distinctly lower throughput after 15 minutes.

Figure 6. **Throughput Profiles for High-fouling Soy Media**

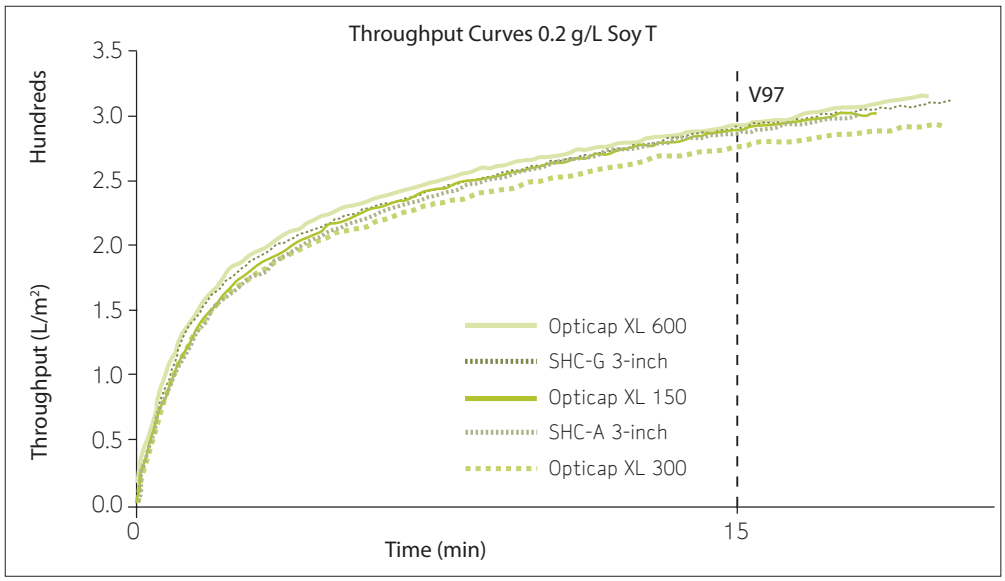
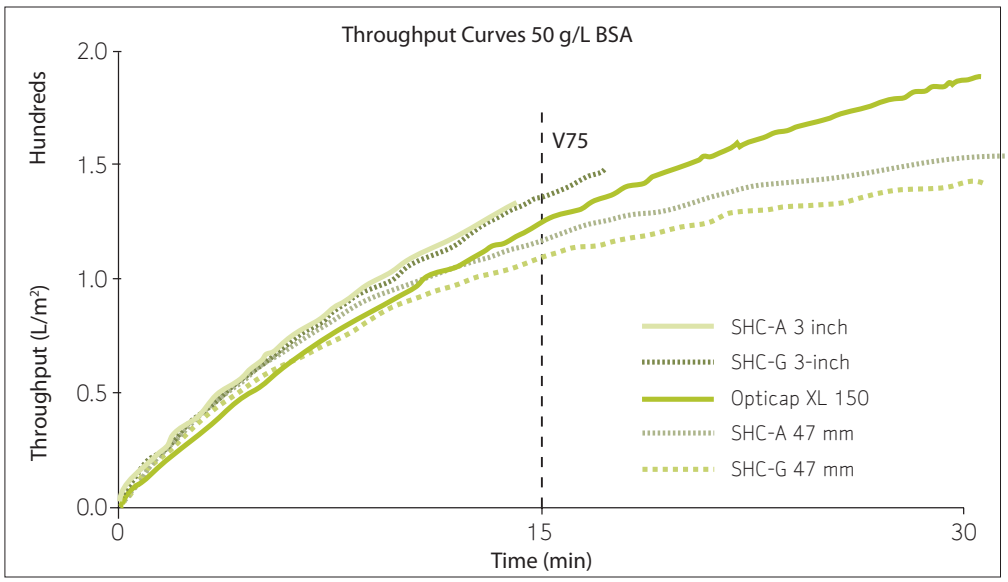


Figure 7. **Throughput Profiles for Low-fouling BSA Media**



DISCUSSION

Table 2 presents the scaling factors for Opticap XL devices with Millipore Express SHC membranes to 10-inch devices. Calculated throughput scaling factors reflect membrane fouling at 97% (V97) and 75% (V75) of the total permeate flux. While all scaling factors are close to unity and demonstrate scalability, these inputs enable the end user to more accurately predict more exact measurement of throughput.

Permeability and Sizing for Flux Based Applications

Opticap XL devices with Millipore Express SHC membranes slightly underestimate the permeability of SHC-A 10-inch devices, as all scaling factors are slightly greater than unity. Opticap XL devices predict SHC-G permeability accurately with less than 10% deviation. This is applicable for non-fouling streams, such as buffers.

Throughput and Sizing for Plugging Feed Steams

Opticap XL devices with Millipore Express SHC membranes accurately predict throughput of SHC-A 10-inch filters within 10% at V97 while throughput at V75 was slightly under estimated as all scaling factors are slightly greater than unity. Opticap XL devices slightly overestimate expected throughput of SHC-G 10-inch filters at V97 and V75, as scaling factors are less than unity.

Several variables can be attributed to the throughput differences among the various device scales; including:

- different structural properties of non-woven support types (polyester vs. polypropylene)
- variability in membrane properties
- media batch variability
- pressure differences due to various fittings and elevations
- test error

SHC-G 10-inch filters and Opticap XL devices contain different support materials. Support material types can provide different flow resistance to effect permeability and throughput under constant pressure test conditions. Also, for high-fouling streams, upstream support material types can vary in their contributions to prefiltration, which in turn affect membrane throughput.

CONCLUSION

Process performance of Millipore autoclavable and gamma-sterilized filters can reliably be predicted for throughput (within 20%) using Opticap XL 150, 300 and 600 small-scale capsules with Millipore Express membranes. Results with water permeability and throughput of two low-to-high fouling streams provided a range of fouling states to mimic bioprocess fluid filtration. Scaling factors, which also accommodate for the different support material types, were determined for more accurate predictions of permeability and throughput.

Table 2. **Scaling Factors Based on Normalized 10-inch Cartridge Data**

		Scaling Factor*					
Device		Permeability		Throughput (0.2 g/L Soy T) V97		Throughput (0.2 g/L Soy T) V75	
Cartridge 10-inch		SHC-A	SHC-G	SHC-A	SHC-G	SHC-A	SHC-G
Express Opticap XL	150	1.18	1.00	0.94	0.83	1.14	0.79
	300	1.13	0.96	0.96	0.85	1.16	0.80
	600	1.08	0.92	0.91	0.81	1.07	0.74

*Scaling factor = 10-inch cartridge/SSC permeability or throughput.

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