



Technical Brief

Scalable Process Filtration with Millipore Express® SHF 0.2 µm Filters

A variety of sizes and formats aimed to scale up your buffer filtration process

INTRODUCTION

Flat disc and small pleated filter devices, such as Opticap® XL 150, 300 and 600 capsules provide convenient formats for low-volume sterile filtration of buffers, pH adjusters and other low-fouling solutions. During buffer filtration process development, filter sizing is typically performed at small scale and scaled to larger devices of the same family using a scaling factor. This technical brief evaluates the scalability of 47 mm discs, Opticap XL 150, 300 and 600 small-scale capsules (SSC) to autoclavable only, gamma sterilizable or presterilized Opticap XL3 and Opticap XL10 filters using Millipore Express SHF (Sterile High-Flux) filters. To assess scalability, permeability at a predetermined test time was measured at all membrane scales using water and 150 mM phosphate buffered saline (PBS).

OBJECTIVE

Define and demonstrate scalability of 47 mm discs to Opticap XL 150, 300, 600, Opticap XL3 and Opticap XL10 pleated filter devices.

METHODS AND MATERIALS

Membranes and Supports

Millipore Express SHF filters contain 0.2 µm polyethersulfone (PES) membrane which provide high flow rates and sterility assurance. These filters are recommended for the sterile filtration of buffers, pH adjusters, cleaning solutions and other low fouling aqueous based streams where the key performance needs are high permeability, process efficiency and bacterial retention.

Millipore Express SHF 0.2 µm filters contain a single layer of membrane sandwiched between two layers of non-woven support material, which support the membrane and provide robustness during processing. Given that customer applications with Millipore Express SHF filters require compatibility with different device sterilization methods, the non-woven support materials vary. Non-woven membrane supports are comprised of either polypropylene, polyethylene or polyester. See Table 1 below.

Table 1. Materials of Construction for Millipore Express SHF 0.2 µm Filters

	Autoclave Only Opticap XL/XLT 3-30 in. capsules	Gamma/Sterile Opticap XL/XLT 3-30 in. capsules	Gamma/Sterile Opticap XL 150, 300 & 600 small-scale capsules
Core	Polysulfone	Polysulfone	Polysulfone
Outer Sleeve	Polypropylene	Gamma stable polypropylene	Gamma stable polypropylene
End Caps	Polypropylene	Gamma stable polypropylene	Gamma stable polypropylene
Membrane Support	Polypropylene	Polyester	Polyethylene
Membrane(s)	Polyethersulfone	Polyethersulfone	Polyethersulfone
O-rings	Silicone Rubber	Silicone Rubber	Silicone Rubber
Capsule Housing	Polypropylene	Gamma stable polypropylene	Gamma stable polypropylene
NaOH Compatibility	Fully compatible >1N	Limited compatibility	Fully compatible >1N

The average effective filtration area (EFA) measured in these trials is shown in Table 2. To determine the test filter's EFA, the filters were cut open and physically measured.

Measured areas of the representative filters were consistent with the reported area and were within 3.5% of the averages listed in Table 2.

Effective area of the 47 mm disc can vary, depending upon the torque method used during holder assembly and the choice of o-ring material. For this study, a consistent torque setting at 25 in-lb and silicone o-rings provided a mean value of 12.9 cm² for 47 mm discs.

All test filters, including 47 mm discs, were from one membrane lot. Opticap XL3 and XL10 capsules were tested as capsule sub-assemblies.

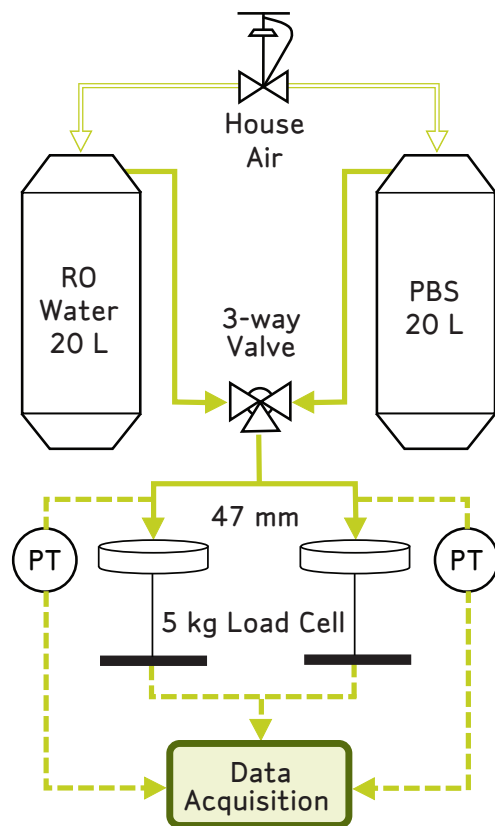
Table 2. Effective Filtration Area (EFA)

Device	Flat disc	Opticap XL capsule			Opticap XL3 capsule		Opticap XL10 capsule	
	47 mm	150	300	600	SHR-A	SHR-G	SHF-A	SHF-G
Area (cm ²)	12.9	220	478	971	1384	1539	4728	5415

BUFFER STREAM

Buffer was prepared in 300-450 liter batches. In an open mixing vessel, phosphate buffer saline (PBS) was prepared by mixing 8.0 g/L sodium chloride, 2.2 g/L sodium phosphate dibasic, 0.2 g/L potassium phosphate monobasic and 0.2 g/L potassium chloride in reverse osmosis (RO) water.

Figure 1. Test System for 47 mm Disk Testing



TEST SYSTEMS

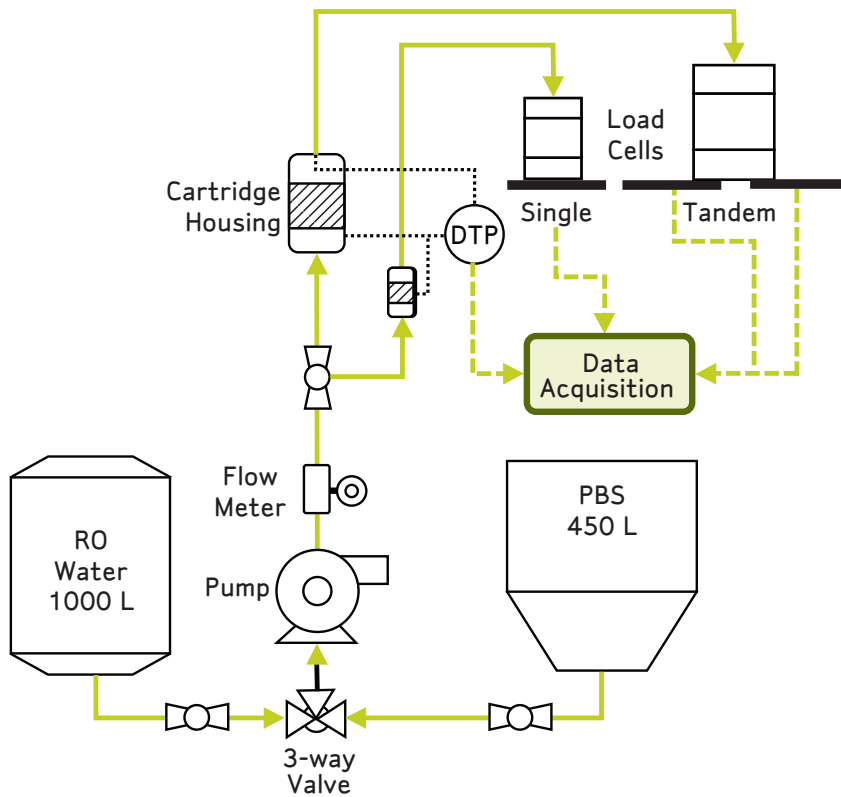
Two systems were used for permeability testing. With each test system, calibrated pressure transducers and calibrated load cells were used to measure pressure and filtrate weight respectively over time. The data was automatically recorded, using a data acquisition system (DAQ). Temperature was recorded manually. Figure 1 shows the test system for 47 mm disc testing. Figure 2 shows the system used for device testing which required a centrifugal pump to deliver the required larger process volumes of water and PBS buffer. Differential pressure across the devices was measured. Tandem load cells were used to collect filtrate weight of the XL3 and XL10 devices.

TEST METHOD

To assess scalability, water and buffer permeability were measured at a predetermined test time for all membrane scales. PBS buffer was selected as the process stream for flux-based testing. Testing the 47 mm disc and various device sizes demonstrated up to ~420 fold scale-up to the Opticap XL10 filter devices.

Piping and devices were purged of air prior to testing. Devices were wet with RO water for at least two minutes at 5–10 psi differential pressure. Following a second purge, water permeability was then measured at 10 psi differential pressure for at least 10 minutes. A three-way valve was used for seamless transfer between water and buffer feed. PBS buffer permeability was measured similarly.

Figure 2. Test System for Device Testing



RESULTS

Water Permeability

Water permeability at 23 °C is summarized in Figure 3. Mean water permeability of 47 mm discs was 1300 lmh/psi (dashed line). The mean permeability values of Opticap XL 150, 300 and 600 devices with Millipore Express SHF membranes were within 19% of 47 mm disc mean permeability. Mean permeability values of autoclavable only (SHF-A) and gamma sterilizable (SHF-G) Opticap XL3 and Opticap XL10 filters also fell within 19% of 47 mm disc mean permeability.

BUFFER PERMEABILITY

PBS buffer permeability at 23 °C is summarized in Figure 4. Mean buffer permeability of 47 mm discs was 1305 lmh/psi (dashed line). The mean permeability values of Opticap XL 150, 300 and 600 devices with Millipore Express SHF membranes were within 19% of 47 mm disc mean permeability. Mean permeability values of the Opticap XL3 and Opticap XL10 filters also fell within 19% of 47 mm disc mean permeability.

Figure 3. Water Permeability

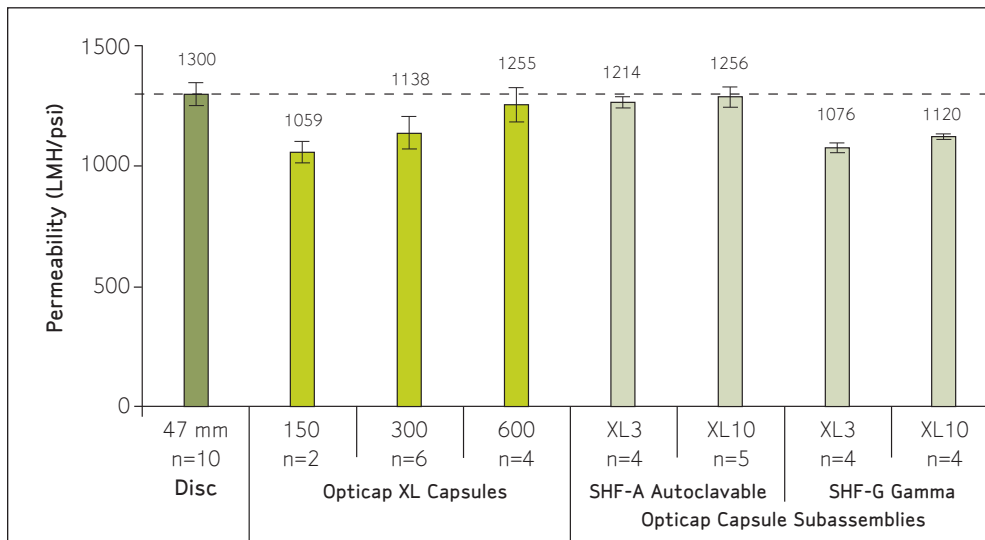
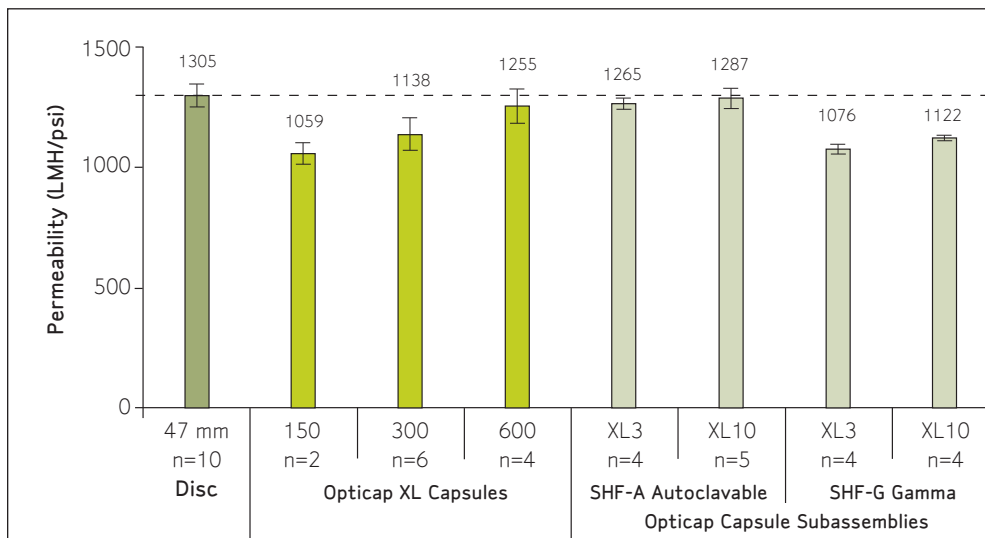


Figure 4. PBS Buffer Permeability



THROUGHPUT PROFILES

Throughput profiles for water are shown in Figures 5 and 6 and for PBS buffer in Figures 7 and 8. Each figure compares filter mean throughput with 47 mm disc mean throughput.

Figure 5. Water Throughput Profiles for Opticap XL 150, 300 and 600 Filters

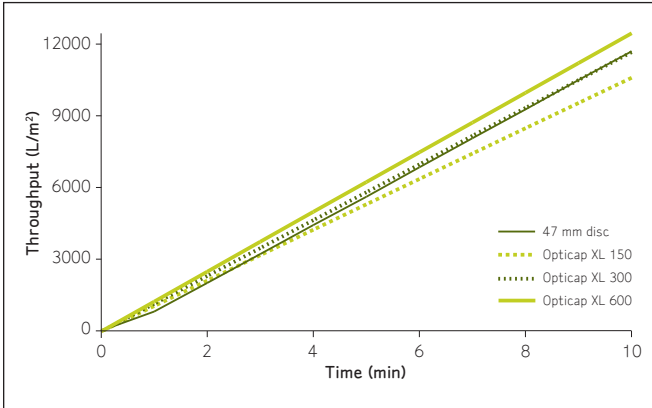


Figure 6. Water Throughput Profiles for Opticap XL3 and Opticap XL10 Filters

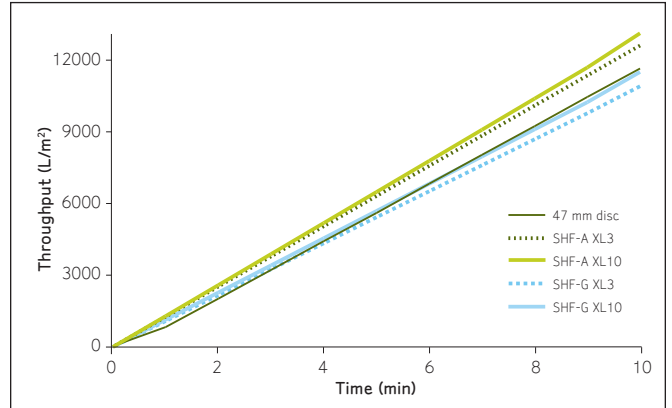


Figure 7. PBS Buffer Throughput Profiles for Opticap XL 150, 300 and 600 Filters

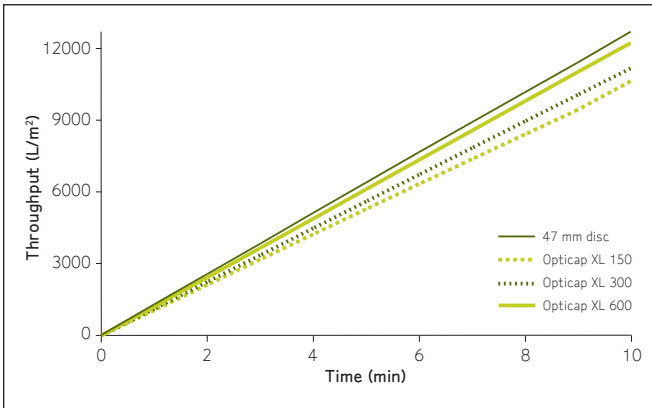
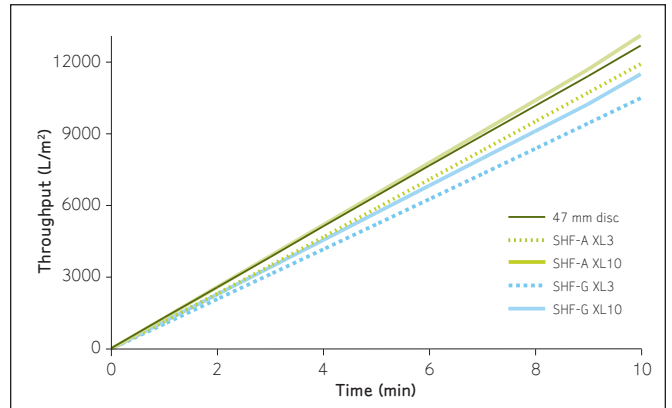


Figure 8. PBS Buffer Throughput Profiles for Opticap XL3 and Opticap XL10 Filters



DISCUSSION

Table 3 presents the scalability of Opticap XL small-scale capsules, Opticap XL3 and Opticap XL10 filters to 47 mm discs with Millipore Express SHF membrane. These values are based on the water and PBS buffer permeability data presented in Figures 3 and 4 and reflect measured filter permeability over a 10 minute test period.

Permeability of autoclavable/gamma sterilizable Opticap XL 150, 300 and 600 devices, gamma compatible Opticap XL3 and gamma compatible Opticap XL10 filters are demonstrated to be within 19% of 47 mm disc performance with water and PBS. Permeability of Opticap XL3 and Opticap XL10 autoclavable capsules are demonstrated to be within 7% of

47 mm disc performance. Given that scalability is based on permeability in this study, these results are applicable for process system sizing with non-fouling streams, such as buffers and some cell culture media additives.

CONCLUSION

For Millipore Express SHF filters, 47 mm disc performance can reliably predict (within 19%) the performance of Opticap XL 150, 300, 600 devices with Millipore Express membranes, Opticap XL3 and Opticap XL10 autoclavable and gamma compatible capsules. Results with water and PBS buffer permeability provided relevant examples of flux-based filtration in biopharmaceutical sterile filtration applications.

Table 3. Scalability to 47 mm Discs*

Millipore Express SHF Device		RO water	PBS
Millipore Express device	150	0.81	0.81
Opticap XL Small-scale capsule	300	0.88	0.85
	600	0.97	0.93
Opticap XL3 capsule	SHF-A (autoclavable only)	0.97	0.93
	SHF-G (gamma sterilizable)	0.83	0.81
Opticap XL10 capsule	SHF-A (autoclavable only)	0.99	0.96
	SHF-G (gamma sterilizable)	0.86	0.86

*Scalability value = Opticap XL 150, 300, 600, Opticap XL3 or Opticap XL10 filter/47 mm disc permeability



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Lit No. TB1798EN00 Rev. A 02/09 Printed in USA. DP SBU-09-01474.
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