Simplifying Progress

A Comparative Study of Polysorbate 80 Adsorption to Membrane Filters for Fill & Finish Applications, Considering a Potentially Upcoming Restriction of PFAS Based Membranes

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Introduction

The final step in biopharmaceutical production, formulation and filling (F&F), requires sterile filtration of the Active Pharmaceutical Ingredient (API) and preservation of its formulation. Traditionally, membrane polymers made of Per- and Polyfluoroalkyl Substances (PFAS), such as Polyvinylidene Fluoride (PVDF) have been preferred in this application due to their favorable adsorption properties for certain excipients such as Polysorbate. However, concerns about the potential impact of PFAS chemicals and polymers on the environment and human health have resulted in proposals to restrict the use of these polymers, highlighting the need for alternative solutions.

1. Experimental Approach

This study describes a comparison of PES- and PVDF-membrane filters, including the newly developed Sartopore Evo® filter for their adsorption properties of Polysorbate 80 (PS80). For a comprehensive evaluation, PES- and PVDF-membrane filters from various manufacturers, in different sizes and formats (flat filter- and pleated devices), were included in the study.

The filters analyzed for their Polysorbate 80 adsorption properties are listed in Table 1. Each filter type was tested in two formats: in a scale-up size with a flat filter format and an effective filtration area (EFA) of 17 to 20 cm² typically used for filter screening trials, and in pilot scale size in a pleated format and an EFA ranging from 200 to 900 cm².

Producer	Filter Typ	Membrane Material
Sartorius	Sartopore 2 0.45/0.2 µm	PES
Sartorius	Sartopore Evo 0.8/0.2 µm	PES
Sartorius	Sartopore Evo 0.2 µm	PES
Merck Millipore	Durapore 0.22 µm	PVDF
Merck Millipore	Express SHC 0.5/0.2 µm	PES
Cytiva	Supor EKV 0.5/0.2 µm	PES
Cytiva	Fluorodyne II 0.2/0.2 µm	PVDF

Table 1: Filter types and membrane materials analyzed for their polysorbate 80 adsorption properties.

All tests were conducted using a placebo solution that mimicked a common drug protein formulation but contained no API (Table 2). The concentration of Polysorbate 80 at 0.1 mg/ml reflects common protein formulation conditions. Furthermore, this low concentration supports the detection of small changes in its concentration in the analyzed filtrate samples.

Formulation Components	Concentration [mg/ml]
Sucrose	80
Polysorbate 80	0.1
L-Histidine Hydrochloride Monohydrate	1.096
L-Histidine	0.741
Water for Injection (WFI)	Ad 1 ml

Table 2: Composition of the test formulation (pH 6.0, Density 1.03 g/ml)

Throughout the entire filtration process, 25 samples (fractionated sampling) of the filtrate were taken for each filter. The Polysorbate 80 concentration of the samples was determined by HPLC analysis providing a comprehensive adsorption profile for each filter tested.

2. Calculation of Polysorbate 80 Adsorption

The total adsorption of each membrane material throughout the entire filtration process was calculated using the following formula:

$$\Gamma = \frac{\sum_{n=1}^{C\sim 100\%} c \cdot V_n \cdot (1 - C_n)}{A}$$

A = Filter surface
c = initial Polysorbate concentration
V = sample volume
C = Measured amount of polysorbates in the sample
Γ = Sum of all adsorption

Figure 1: Formula to calculate Polysorbate 80 adsorption.

In addition, the filtrate volumes to recover 90, 95 and 98 % of the initial Polysorbate 80 concentration of the formulation were derived from the analytical data, to determine potentially required flush volumes for each filter.

3. Results – Examples of Polysorbate 80 Binding Curves

Figures 2 to 8 illustrate the specific adsorption profiles of the tested filters depicting the relationship between the relative concentration of Polysorbate 80 in the filtrate (compared to 0.1 mg/ml in the starting solution) and the volume filtered per filter area (l/m²) for the pilot-scale filters.

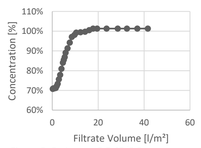

Figure 2: Sartopore 2 0.45/0.2 µm

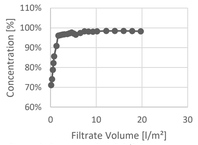

Figure 3: Sartopore Evo 0.8/0.2 µm

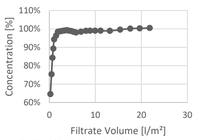

Figure 4: Sartopore Evo 0.2 µm

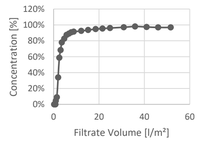

Figure 5: Express SHC 0.5/0.2 µm

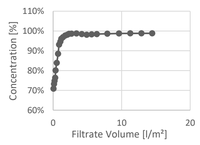

Figure 6: Durapore 0.22 µm

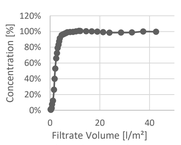

Figure 7: Fluorodyne II 0.2/0.2 µm

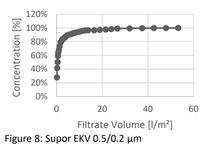

Figure 8: Supor EKV 0.5/0.2 µm

4. Results – Polysorbate 80 Binding

Producer	Filter Typ	Material	Scale-Up Filter [mg/m²]	Pilot Scale Filter [mg/m²]
Sartorius	Sartopore 2 0.45/0.2 µm	PES	291	146
Sartorius	Sartopore Evo 0.8/0.2 µm	PES	63	66
Sartorius	Sartopore Evo 0.2 µm	PES	37	36
Merck Millipore	Durapore 0.22 µm	PVDF	64	35
Merck Millipore	Express SHC 0.5/0.2 µm	PES	363	453
Cytiva	Supor EKV 0.5/0.2 µm	PVDF	383	234
Cytiva	Fluorodyne II 0.2/0.2 µm	PES	147	191

Table 3: Summary of Polysorbate 80 adsorption results across various filter types and formats.

5. Results – Polysorbate 80 Recovery

Depending on the specific adsorption properties of each filter, a certain product volume is required to recover the initial concentration of Polysorbate 80 in the formulation. Figure 9 summarizes the filtrate volumes required to recover 90, 95 & 98% of the initial Polysorbate 80 concentration for the pilot scale (pleated devices) filters.

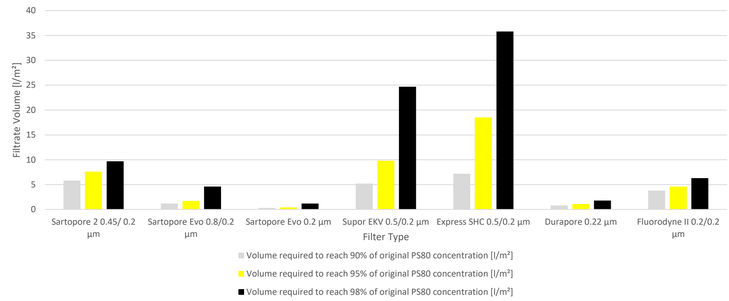

Figure 9: Summary of the product volumes required to recover 90, 95 & 98% of the initial Polysorbate 80 concentration in the formulation (pilot scale filters).

6. Summary & Conclusion

- The potential ban of PFAS polymer-based membrane filters necessitates identifying alternative filter materials with minimal adsorptive properties for biopharmaceutical form and fill processes.
- This comprehensive comparison of PES and PVDF filters revealed substantial differences in Polysorbate 80 adsorption, highlighting the critical role of membrane surface modification over polymer class in determining a membrane's suitability for sterile filtration in form and fill processes.
- Notably, Sartopore Evo® single- and double layer PES filters, carrying a newly developed membrane surface modification, exhibited significantly low Polysorbate 80 adsorption, comparable or better to PFAS based membrane filters.
- Consequently, a fast recovery of the initial Polysorbate 80 concentration in the filtered formulation is achieved, minimizing potential product loss in commercial filling operations.
- While this poster focuses on Polysorbate 80 adsorption data, additional data is available for other excipients such as Polysorbate 20 and Poloxamer 188 as well as protein binding (e.g.: Monoclonal Antibodies) in actual product formulations, which confirm the general low binding properties of Sartopore Evo.
- Combining excellent filtration performance with low adsorption properties for proteins and excipients, position Sartopore Evo® as a suitable alternative to PFAS based membrane filters for reliable and efficient final sterile filtration of protein-based formulations.