ECI Vaccine Technology VI
Albufeira, Portugal
12-17 June 2016

Custom Open Polyethersulfone Ultrafiltration Membranes for Vaccines

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Introduction

Vaccines save millions of lives every year, and improve the quality of life for countless others. In conjugated polysaccharide (CPS) vaccines like Prevnar 13®, Menactra®, and ActHIB® for pneumonia and meningitis, bacterial polysaccharides (PS) are chemically linked or conjugated to carrier proteins (CP), e.g. diphtheria or tetanus toxoid to enhance the immune response beyond that of the PS alone. Ultrafiltration (UF) membranes are used for the concentration and purification of each component, and are critical for the supply of vaccines worldwide.

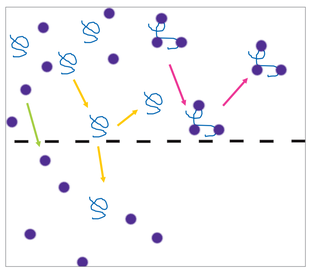
In multivalent blends, the CP, each PS, and each CPS is produced by a separate process. The CP and PS require tighter membranes than the related CPS. Biomax® 100kD and Biomax® 300kD membranes are often used for PS and CPS vaccines. There is a need for additional variants between the two.

Recent process improvements now enable us to make targeted variants. This poster presents data for the retention of pneumococcal polysaccharide model streams by some of these variants.

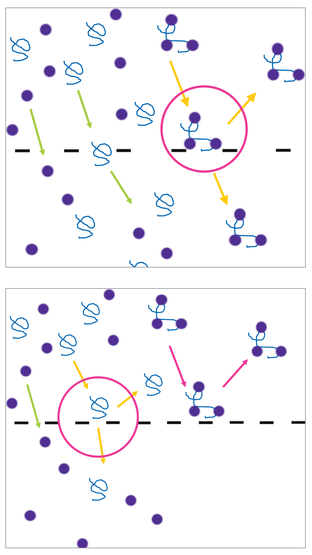
Description

A UF membrane retains larger species and passes smaller ones. In CPS vaccines, the CPS is not much larger than the PS, and both have a range in size… these may overlap.

An ideal pore size allows acceptable passage of unreacted PS and CP with high retention of the CPS.



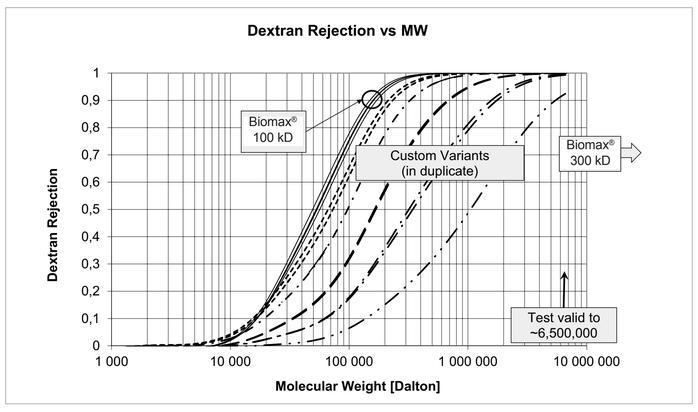
Larger pores allow higher passage of the conjugate, and reduces the yield.



Smaller pores increase yield, but also increase the impurity level.

Characterization by Mixed Dextran Rejection[1]

- Challenge: rejection of dextrans of different molecular weight (mw) in stirred cells
- Assay: fractionation by size exclusion chromatography (SEC) with refractive index (RI) detection
- Rejection calculated from feed and permeate concentrations at each mw
- Characterized by mw of dextran rejected at 90%, 75%, and 50%. Curves for some PES UF membranes shown below.



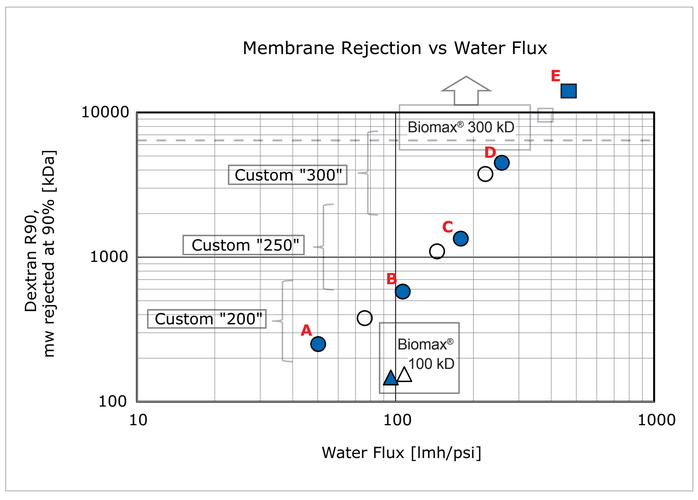
[1] Tkacik, G. and Michaels, S., (1991) Bio/Technology 9, 941-946

Batch Diafiltration

Batch diafiltration of pneumococcal polysaccharides in stirred cells.

Membranes:

Biomax® 100kDa and 5 custom variants, denoted by the blue filled symbols.



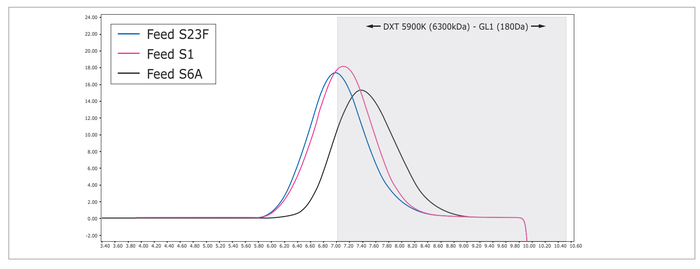
Challenge:

- Serotypes S1, S6A, and S23F at 0.5 mg/ml in PBS
- 20 lmh (liter/(m²-hr) permeate flux, 350 rpm stir rate
- 50% volume reduction, reconstitution with buffer, repeat
- Permeate and retentate samples collected for assay
- Assay: SEC with RI detection
- Retentate and permeate concentration ratios calculated from peak areas

Results and Discussion

The three polysaccharides are large, and have wide mw distributions.

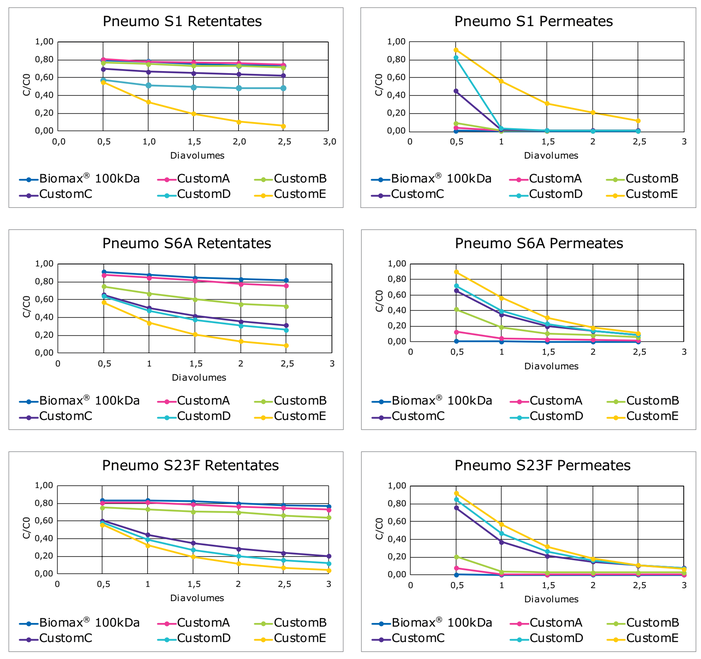
- S1: low 20kD, mid 4200kD
- S6A: low 20kD, mid 1650kD
- S23F: low 20kD, mid 6500kD



The figures show the ratios of the concentrations in each retentate and permeate sample, relative to the initial concentration in the original feed, for each serotype.

The Biomax® 100kD sample is the "tightest" variant, and retains the most. The CustomE variant is the most "open" in the series, and passes the most. The variants in between exhibit intermediate performance, in rank order.

Separations with real feeds are more complicated, but having the ability to target membrane performance to the application can lead to better yields and purity.



Conclusions

- Targeted variants have been used with actual vaccine components to show how they can be used to identify appropriate candidates for a desired separation.
- New membrane variants could be used as new, independent products to match specific customer needs.

Summary

An improved process for making open polyethersulfone (PES) ultrafiltration membranes has been developed, enabling more precise targeting of membrane properties.

Applications include polysaccharide and polysaccharide-conjugate vaccines, and potentially processes containing surfactant micelles and virus-like particles (VLP).

We welcome customer collaborations for the evaluation of these membranes.

PS3154EN00 Ver. 1.0