SARTORIUS

Application Note

May 01, 2011

Host Cell Protein Removal

A Comparison Between Sartobind STIC® PA and Sartobind® Q

Dr. Ricarda Busse, Dr. Miyako Hirai, Dr. Carsten Voss
Sartorius Stedim Biotech GmbH, August-Spindler-Straße 11, 37079 Göttingen, Germany

Correspondence
E-Mail: ricarda.busse@sartorius.com, miyako.hirai@sartorius.com, carsten.voss@sartorius.com

Introduction

In anion exchange flow-through (FT-AEX) applications, membrane chromatography offers higher throughput, less buffer consumption, and more convenient handling than traditional bead columns. Conventional quaternary amine based chemistries – although established as a standard FT polishing step in Monoclonal Antibody (MAb) purification processes – typically require low feed conductivity. This often involves dilution of feedstreams and can result in facility fit limitations when high titer processes are accommodated in existing plants[1]. Furthermore, high impurity levels limit load densities and would require larger membrane adsorber volumes and lead to increased production cost. To address these limitations and facilitate a wider design space for FT-AEX membrane chromatography at commercial scale, Sartobind STIC® (Salt Tolerant Interaction Chromatography), a novel membrane concept based on weak anion exchange chemistry was developed[2]. The Sartobind STIC® PA (primary amine) anion exchange membrane is composed of a primary amine ligand that is attached to a cross-linked, regenerated macroporous cellulose base matrix.

The superior performance of Sartobind STIC® PA membrane at higher conductivities can be attributed to the ligand and ligand density. It is important to note that while the working pH of quaternary amine chemistries are ~pH 8, the weak anion exchange ligand of Sartobind STIC® PA may require operating at a lower pH for optimal impurity clearance.

Find out more: www.sartorius.com/en/products/lab-filtration-purification/membrane-chromatography

Materials

Membrane	1) Sartobind STIC® PA 2) Sartobind® Q
Membrane ligand	1) Primary Amine (PA) 2) Quaternary ammonium (Q)
Membrane volume (area)	0.41 mL (15 cm^2)
Number of membrane Layers	3
Load material (HCP) concentration	500 ppm (500 ng HCP/mg MAb)

Method

A MAb feedstream produced in CHO (Chinese Hamster Ovary) cell culture was processed through affinity and cation exchange chromatography steps before being processed through either Sartobind STIC® PA or Sartobind® Q under flow-through conditions. Sartobind® Q was loaded at pH 8 and a conductivity of 7 mS/cm, while Sartobind STIC® PA was loaded at pH 8 and at conductivities of 7, 10 and 15 mS/cm. The MAb feedstream had a host cell protein (HCP) concentration of 500 ppm (500 ng per mg of MAb), and was loaded at a rate of 10 membrane volumes/minute, up to a load density of 10 kg/L of membrane volume[3]. HCP levels were measured in the filtrate at various intervals.

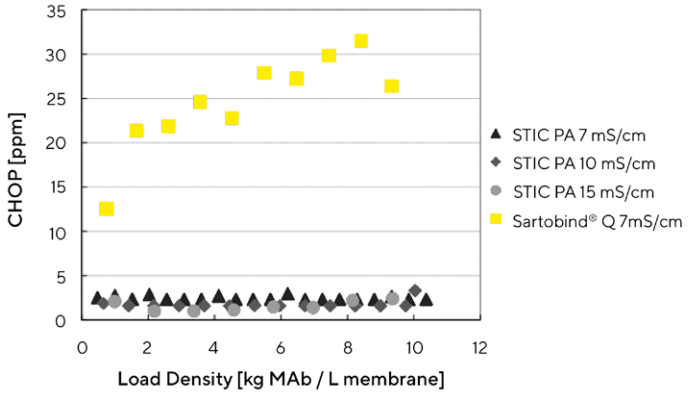

Fig. 1: HCP concentration in Sartobind STIC® PA and Sartobind® Q pools as a function of load density at various conductivities. Sartobind STIC® PA shows higher HCP clearance than Sartobind® Q at conductivities up to 15 mS/cm.

Results

Figure 1 shows the superior HCP clearance with Sartobind STIC® PA as compared to Sartobind® Q. At a load condition of pH 8, 7 mS/cm, Sartobind® Q showed increasing levels of HCP in the pool through the entire duration of load while Sartobind STIC® PA cleared HCP to less than detectable at a load density up to 10 kg/L. At higher conductivity conditions, 10 and 15 mS/cm, Sartobind STIC® PA also cleared HCP to less than detectable at a load density up to 10 kg/L. This exemplifies the ability of Sartobind STIC® PA to operate at high conductivity conditions without adverse impact to HCP clearance.

Summary

Sartobind STIC® PA is able to overcome the limitations of HCP removal at high conductivities by utilizing a primary amine ligand that is attached to a cross-linked, regenerated macroporous cellulose base matrix. This novel combination results in higher binding capacities of impurities at high conductivities, which may eliminate facility fit limitations caused by feedstream dilution when using adsorbers that necessitate operating at low conductivities.

References

1. Faber, R., Yang, Y. & Gottschalk, U. Salt tolerant interaction chromatography for large-scale polishing with convective media. BioPharm Int. Suppl. 11–14 (2 October 2009).

2. Fraud, N., Shomglin, K., Faber, R., van Reis, R., Gottschalk, U. & Mehta, A. New membrane adsorber for polishing at high salt concentration. Recovery of Biological Products XIV Conference Lake Tahoe, California, USA, 1–6 August 2010

3. Fraud, N., Faber, R., Mehta, A., Tully, T., Ultra small membrane adsorbers for process development & screening of new membrane adsorbers. 238th ACS Meeting, Washington August 16–20, 2009.

Germany
Sartorius Stedim Biotech GmbH
August-Spindler-Strasse 11
37079 Goettingen
Phone +49 551 308 0

USA
Sartorius Stedim North America Inc.
565 Johnson Avenue
Bohemia, NY 11716
Toll-Free +1 800 368 7178

For further contacts, visit
www.sartorius.com

Publication No.: SL-4060-e | Order No.: 85032-540-18 | Status: 08 | 25 | 2021