sartorius stedim biotech

Host cell protein removal with Sartobind STIC® PA pico

Performance of salt tolerant anion exchanger in a miniaturized capsule format

Application Note

Materials

Membrane	Sartobind STIC PA
Membrane ligand	Primary Amine (PA)
Membrane volume (area)	0.08 ml (2.9 cm^2)
Bed height	4 mm
Load material host cell protein concentration	303 ppm (303 ng HCP/mg MAb)
Connectors	Luer female

Introduction

Application

In anion exchange flow-through (FT-AIEX) 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[1,2]. Furthermore, high impurity levels limit load densities and would require larger membrane adsorber volumes and lead to increased production cost.

Membrane

To address these limitations and facilitate a wider design space for FT-AIEX membrane chromatography at commercial scale, Sartobind® STIC (Salt Tolerant Interaction Chromatography), a 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.

Device

Material consumption is often critical during testing and in early development stages. To reduce sample usage when testing Sartobind STIC, the Sartobind pico (see upper figure) device was developed. With a membrane volume of 0.08 ml and a 4 mm bed height, it is the smallest scalable capsule in the Sartobind STIC 4 mm capsule family.
The device can be operated by hand with a syringe or in a liquid chromatography system via finger tight Luer Lok adapters.

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 Sartobind STIC PA under flow-through conditions. Sartobind STIC PA was loaded at pH 7.0 and at a conductivity of 11 mS/cm. The MAb feedstream had a host cell protein (HCP) concentration of 303 ppm (303 ng per mg of MAb), and was loaded at a rate of 10 membrane volumes/minute, up to a load density of 10 kg/liter of membrane volume[3]. HCP levels were measured in the filtrate at various intervals.

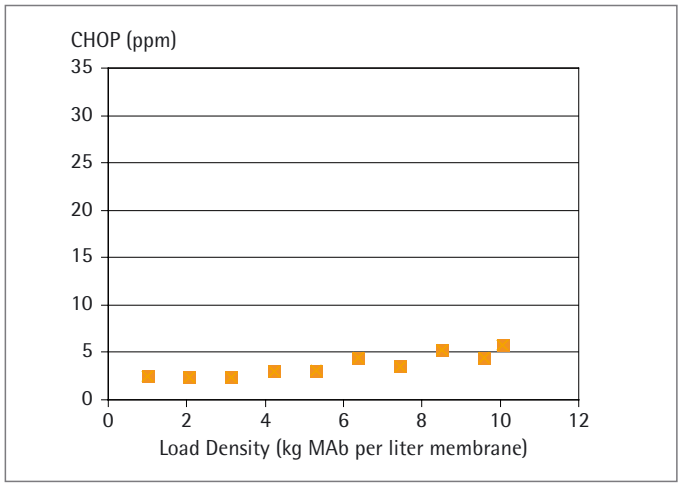

Fig. 1: HCP concentration in Sartobind STIC PA pico pools as a function of load density

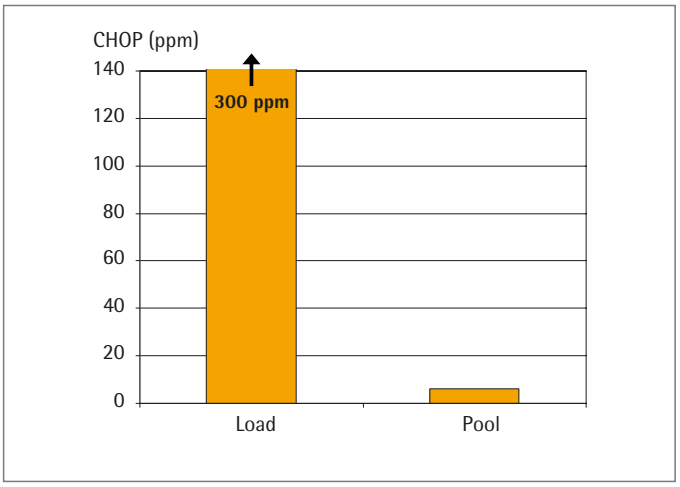

Fig. 2: HCP reduction at targeted load of 10 kg MAb per liter membrane

Results

Figures 1 and 2 show the HCP clearance with Sartobind STIC PA. At a load condition of pH 7, 11 mS/cm, Sartobind STIC PA cleared HCP to less than 6 ppm at a load density up to 10 kg MAb per liter membrane adsorber. 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 can resolve facility fit limitations caused by feedstream dilution when using chromatography media that necessitates operating at low conductivities. The Sartobind pico design with 4 mm bed height allows for >10 times reduced sample consumption and substantial cost savings for virus validation studies as compared to Sartobind nano with 1 ml membrane volume.

References

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