Comparison of the Performance of Resin and Membrane Chromatography Platforms for Monoclonal Antibody Purification

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ABSTRACT

Advancements in upstream monoclonal antibody (mAb) production have made downstream purification bottlenecks ever more pronounced. The industry has long sought a high productivity purification platform to reduce development timelines, expand manufacturing capacities, and improve process economics. However, while widely implemented resin columns provide solid purification performance, they do so at the expense of process productivity, due to their slow flow rates and high cost. Traditional membrane chromatography provides high throughput in a disposable format, but has found limited acceptance due to its low binding capacity.

Natrix Separations has developed a hydrogel membrane technology that combines high binding capacity with high throughput to deliver a new combination of performance for mAb purification. This poster illustrates a performance comparison between traditional resin-based methods and an entirely single-use Natrix membrane-based platform. The results presented here highlight the potential of single-use chromatography alternatives in mAb purification processes.

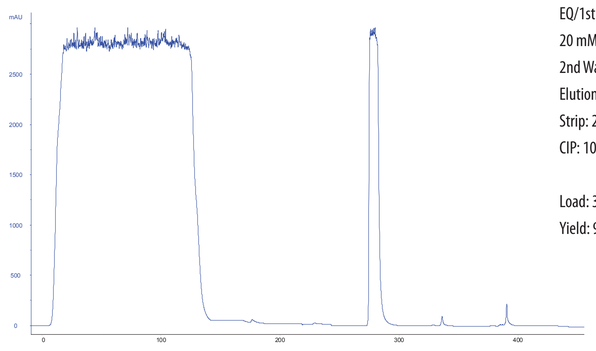
INTRODUCTION

Combining disposable devices with a platform approach allows monoclonal antibody (mAb) manufacturers to achieve rapid and generic process development while enabling flexibility and efficient use of resources. Natrix Separations has created the foundation for such a single-use purification toolset and is making rapid progress toward a complete downstream platform.

Designed for capture and intermediate purification steps, Natrix HD-C (experimental weak cation exchanger) and Natrix HD-Sb (strong cation exchanger with hydrophobic modality) enable fast flow rates with high binding capacity as well as multi-cycle capability to optimize process economics. Designed for flowthrough operation, NatriFlo HD-Q (strong anion exchanger) is able to process very high loads at fast flow rate and maintains exceptional impurity reduction over a wide range of operating conditions. When incorporated into purification platforms, Natrix hydrogel membrane devices help to further reduce the process cycle time and decrease capital costs. A performance comparison between a traditional resin-based platform and an entirely single-use Natrix membrane-based platform is presented here to discuss the potential and productivity advantage of single-use chromatography alternatives in mAb purification processes.

CASE STUDY: PURIFICATION OF 600 G OF MAB WITH TRADITIONAL AND SINGLE-USE PLATFORM

Protein A Column



Buffer conditions
EQ/1st Wash/3rd Wash: 20 mM NaCl in 20 mM BIS-TRIS, pH 7.4
2nd Wash: 1 M NaCl in 20 mM BIS-TRIS, pH 7.4
Elution: 20 mM NaCl in 20 mM BIS-TRIS, pH 3.5
Strip: 200 mM Acetic Acid
CIP: 100 mM NaOH

Load: 30 g/L
Yield: 95%

Elution Pool
HCP Level = 953 ppm
Aggregate Level = 3.41%

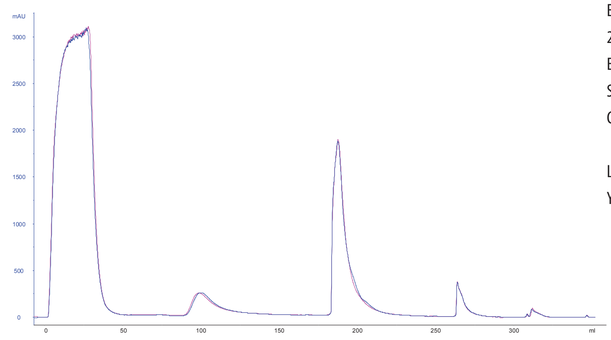
CAPTURE
8.5 hours

Protein A resin 6 L: 4 cycles
Natrix HD-C 500 mL: 20 cycles

Protein A Column
Media Volume 6 L

Natrix HD-C
Media Volume 500 mL

HD-C Weak CEX Membrane

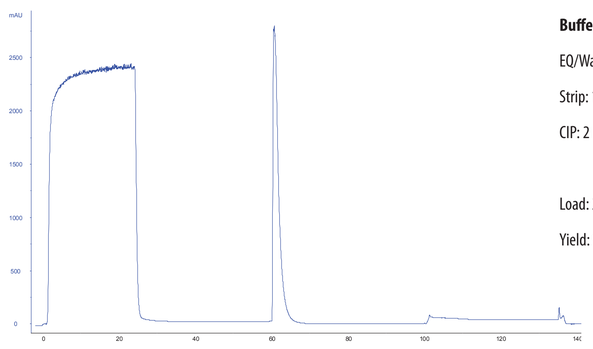


Buffer conditions
EQ/1st Wash: 50 mM NaOAc, pH 5.0, 13 ms/cm
2nd Wash: 30 mM MES, pH 6.5
Elution: 110 mM MES, pH 6.5
Strip: 1 M NaCl in 200mM Phosphate, pH 7.5
CIP: 1 M NaCl in 30mM NaOH

Load: 70 g/L
Yield: 85%

Elution Pool
HCP Level = 1,329 ppm
Aggregate Level = 2.90%

Strong AEX Column



Buffer conditions
EQ/Wash: 25 mM TRIS, pH 8.1
Strip: 1 M NaCl in 25 mM TRIS, pH 8.1
CIP: 2 M NaCl in 1 M NaOH

Load: 200 g/L
Yield: 98%

FT Pool
HCP Level = 588 ppm
Aggregate Level = 3.04%

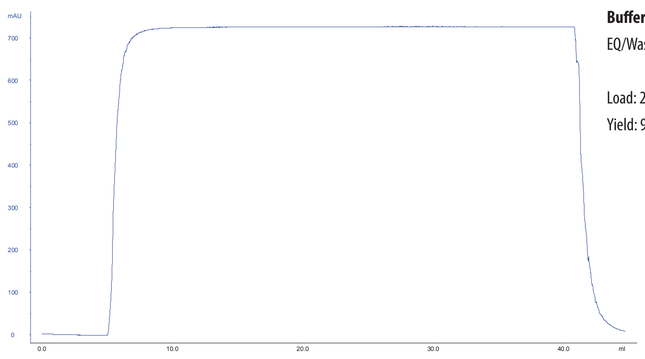
INTERMEDIATE POLISHING
2 hours

AEX resin 2 L: 2 cycles
Natrix HD-Q 115 mL: 2 cycles

AEX Column
Media Volume 2 L

Natrix HD-Q
Media Volume 115 mL

HD-Q Strong AEX Membrane

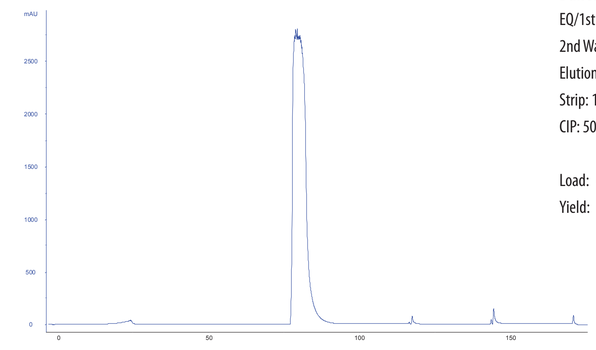


Buffer conditions
EQ/Wash: 25 mM TRIS, pH 8.1

Load: 2000 g/L
Yield: 98%

FT Pool
HCP level = 528 ppm
Aggregate level = 1.14%

Mixed Mode Column



Buffer conditions
EQ/1st Wash: 50 mM NaOAc, pH 4.5, 16 ms/cm
2nd Wash: 20 mM Phosphate, pH 6.5
Elution: 20 mM Phosphate, pH 6.5, 15 ms/cm
Strip: 1 M NaCl in 25 mM TRIS, pH 8.2
CIP: 500 mM NaOH

Load: 65 g/L
Yield: 95%

Elution Pool
HCP Level = 29 ppm
Aggregate Level = 2.90%

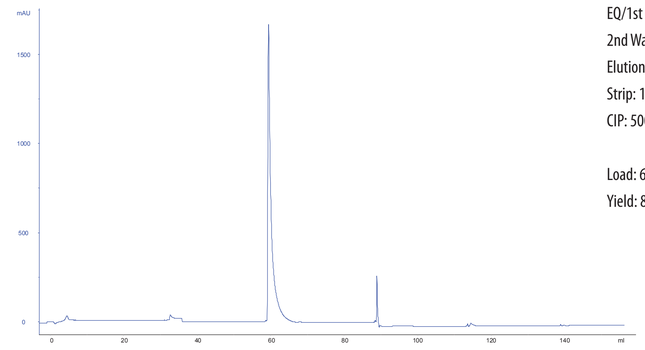
FINAL POLISHING
9 hours

Mixed-Mode resin 3 L: 3 cycles
Natrix HD-Sb 500 mL: 18 cycles

Mixed Mode Column
Media Volume 3 L

Natrix HD-Sb
Media Volume 500 mL

HD-Sb Strong CEX + HIC Modality



Buffer conditions
EQ/1st Wash: 50 mM NaOAc, pH 4.5, 16 ms/cm
2nd Wash: 20 mM Phosphate, pH 6.5
Elution: 20 mM Phosphate, pH 6.5, 6 ms/cm
Strip: 1 M NaCl in 25 mM TRIS, pH 8.2
CIP: 500 mM NaOH

Load: 65 g/L
Yield: 85%

Elution Pool
HCP level = 36 ppm
Aggregate level = 0.53%

ABOUT NATRIX SEPARATIONS

Natrix Separations is the developer and manufacturer of Natrix HD membrane technology, an advanced chromatography material that enables significant speed and capacity improvements for the capture and purification of biologics. Natrix products utilize established industry-standard chemistries in a single-use format to provide a low cost manufacturing advantage for drug developers. The Natrix team is comprised of industry leaders in downstream processing, as well as engineering, design, quality and manufacturing. Natrix is privately-held and based in Burlington, Ontario, Canada.

About Natrix Technology

Natrix HD Membranes offer a breakthrough in membrane architecture that will change downstream purification. With a three-dimensional macroporous hydrogel structure that provides a High Density of binding sites and rapid mass transfer, Natrix HD Membranes deliver binding capacity that exceeds resin-based columns with the fast flow rates typical of membrane adsorbers. Additionally, Natrix HD Membrane technology is highly versatile, and can be deployed in flow-through or bind-elute mode, with nearly any ion exchange, affinity or customized chemistry.

CONCLUSION

This study shows how a combination of several single-use high productivity materials can be used to develop a simple and robust monoclonal antibody purification process to replace a traditional resin based process. This process performs as well as, or better, as a traditional process. In addition, a fully disposable single-use process significantly reduces both regulatory and financial exposure during process development and clinical manufacturing.