Affinity Membrane Chromatography Platform to Optimize Purification Process Architecture

ABSTRACT

As the only purification technique that enables biomolecule separation based on individual biological and chemical structure, affinity chromatography can easily achieve a high degree of purity that would otherwise require a complicated process combining other techniques. The process success of the widely accepted Protein A affinity resin column in monoclonal antibody (mAb) manufacturing has demonstrated the ease of method development and the potential for a generic purification approach using affinity chromatography. Unlike resin manufacturing, many biopharmaceutical segments still use traditional purification schemes that suffer from long lead and lengthy processing times because multiple unit operations have to be employed together to achieve the desired purity due to the lack of suitable affinity media. This work presents an emerging technology platform that combines high selectivity with the high productivity of Natrix hydrogel membranes, while leveraging all the proven benefits of single-use technologies. This poster presents three proof of concept studies demonstrating optimized process architectures with ligands specifically designed for mAbs and vaccine purifications. The best all-purposes chromatography performance of the Protein A membrane is comparable to the reference resin column (~1.4 LRV), while the novel Affilin® membrane shows excellent impurity reduction for both yeast and HEK293 harvests (~4 LRV and 3.3 LRV, respectively). As a result, the number of steps is reduced as compared to the reference processes (from 3 to 2 chromatography steps using the Protein A membrane and down to one chromatography step using the Affilin® membrane).

NATRIX HD MEMBRANE TECHNOLOGY

Membrane Generation
- Flexible, monofilament fiber mesh provides strength and structure
- Made by winding monofilament yarns into a monofilament loom
- Fatigue-resistant, fabric-like composite membrane is created in a single step

Membrane Characteristics
- Highly-permeable binding groups and final pore structure
- Identical final circuit binding group chemistry as resin – C, Q & S

Advantages
- High ligand density provides high binding capacity
- No BSA limitation allows for residence time in seconds
- Fully disposable and suitable for GMP manufacturing

About Natrix Technology:
Natrix HD Membranes offer a breakthrough in membrane architecture that will change downstream purification. With a three-layered HD-A Membrane, Engineered Membrane, Polymer Nanoparticles and HD-A Membrane, the engineered ligands are coupled with the Natrix-HD membrane technology an even more efficient process is obtained. This new affinity material provides better process comparison for both yeast and HEK293 harvests (4.6 LRV and 3.3 LRV, respectively). As a result, the number of steps is reduced as compared to the reference processes (from 3 to 2 chromatography steps using the Protein A membrane and down to one chromatography step using the Affilin® membrane).

Table 1: Best-in-class Impurity Clearance for Multiple HKR

Table 2: Robust Impurity Clearance Across Multiple Buffer Systems

Table 3: Capture – >99.9% Pure EGFR in a Single Step

Table 4: Capture – >99.9% Pure EGFR at Most Difficult Feed

PROTEIN A MEMBRANE

Ligand: Protein A Ligate
MW = 42 kDa

Target: IgG
MW: 150 kDa

About Natrix Separations:
Natrix Separations is the developer and manufacturer of Natrix® HD Membrane Technology, an advanced chromatographic material that enables significant speed and capacity improvements for the capture and purification of biologics. Natrix products utilize established industry standards 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.

PRODUCT INFORMATION

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COMCLUSIONS

Combining the benefits of specifically engineered ligands with single-use membrane adsorbers provides numerous advantages for optimizing mAb and vaccine purification. The high specificity of the ligand increases the process purity which reduces the need for multiple purification steps. As demonstrated with the Natrix HD-A affinity membrane, the CEX step following Protein A capture and removal and mAb purification is reduced from a 3 chromatography step process to a 2 chromatography step process. In the vaccine production case study, incorporating Affilin® membrane enables a simplified upstream and downstream process of only 11 steps compared to 26 steps in the original manufacturing process. This simplified process architecture increases yield as well as reduces the cost of goods. When the engineered ligands are coupled with the Natrix-HD membrane technology, an even more efficient process is obtained. This new affinity material provides better or equal impurity clearance with the increased advantages of higher productivity (6 second residence times) and process robustness. Natrix hydrogel membranes add flexibility and reduce the cost of goods in mAb and vaccine purifications. The attributes of this emerging technology platform are a better fit towards being competitive in biosimilar markets as well as competing with global markets.

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