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innovative continuous chromatography

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XPure-R: A Rapid Resin Aging System (RRAS) for Holistic Development of Adsorption Processes

Introduction

Over the past six decades, adsorption processes have been established in separation industries, and the applications are ever-growing. Chromatography adsorption has become an integral part of separation industries, and they continue to invest and conduct research to improve its cost efficiency and process effectiveness. Resins or adsorbents are the backbones of chromatography processes and they have major effects on the process's efficiency.

During the research phase, a careful methodology ensures the meticulous screening of the resins for desired product separations. However, the durability of the resins remains a question unless experiments are performed until the end of resin life. This is time-consuming and expensive, increasing R&D costs. Although resin manufacturers specify the life of the resins, the actual durability is highly process-specific. Most importantly, as resins are costly, the industry needs to run the packed column for the maximum number of cycles possible to reduce the cost of processing. Even if the studies are performed on a small scale, they can never mimic the variability on a large scale, causing an error in the aging analysis.

Several factors further complicate the issue. Resins for specialized chromatography processes such as expanded bed adsorptions (EBA) have never been subjected to aging studies. With no prior data available, it is almost impossible to make the most economical choice. In addition, the resin aging data has become a requirement for the regulatory authorities in biopharmaceutical industries (Anurag Rathore, 2003).

Now that it has become clear that there is no practical way to bypass the resin testing, the question is how industries will make it cost-effective. Does it make sense to use a platform? If so, which perform can sustain automated testing for the experimentalists using the least time and resources, while giving the most accurate data on resin life? This is what we offer with XPure–R Rapid Resin Aging System (RRAS).

Basics of Resin Aging

In most chromatography processes, it is common that resins are exposed to different processing conditions of feed streams, wash buffers, elution buffers, and cleaning liquids to bind, wash, elute, and clean respectively. Every chromatography cycle must ensure complete cleaning of the resin before the next cycle is started. Feed streams can be particulate or viscous, whereas; fermentation broths or partially clarified feeds are direct inputs on adsorptive beds. This is the case with expanded beds.

These conditions can lead to fouling, which calls for a thorough cleaning process in order to renew the resin surface for subsequent cycles. However, the cleaning processes used are quite harsh and over time, they deteriorate the resins separation efficiency, resulting in aging.

Performance decay is a result of the inaccessibility of pores, change of pore structures, leaching of ligands, or active sites, etc. (Mauryn Nweke A. r., 2018). Different resins respond differently to the processing variables, cleaning procedures, packing methods, etc. and show different aging patterns according to their base material and ligand configurations (Mauryn Nweke G. M., 2017). Studying aging of the resin at actual process conditions can facilitate decision-making at important junctures of process development, which can then scale up.

For example, post-screening, two resins, A and B, are shortlisted based on binding and elution studies. Resin aging studies showed the following performance parameters for a product with a requirement of purity >97.5%;

Resin Type	Pre-aging studies (0 cycles)		After 100 cycles		After 200 cycles		Aft
	Purity (%)	Yield (%)	Purity (%)	Yield (%)	Purity (%)	Yield (%)	Purity (%)
Resin A	99.5	98.1	98.4	96.3	97.3	74.5	90.3
Resin B	98.7	97.3	98.6	95.7	98.3	94.3	97.9

From start to 100 cycles, resin A showed superior performance. For the next 100 cycles, resin B was found to be more consistent in meeting the requirements, whereas resin A dropped marginally. The difference became clearer after 400 cycles, where resin A clearly underperformed in both purity and yield; however, resin B showed a marginal drop in yield but retained purity.

Assuming both resins have the same cost if the selection was made without aging studies, resin A would be preferred. However, it is clear that resin B is certainly a better choice for long term returns for both quality and yield as it is more consistent in performance for a higher number of cycles. This shows that aging studies are significant in deciding the resin before detailed process development and scale-up. If the efforts are invested in the second-best option (resin A here), it will be a continuous invisible loss, which will never be realized.

Features of XPure-R: RRAS

XPure-R, also called Rapid Resin Aging System (RRAS), allows the user to perform experiments at a smaller scale, making it possible to assess resin performance under actual process conditions, over many cycles, within a shorter timeframe, and with fewer input materials. Shorter cycle times are achieved by splitting the single column further down into smaller parts while processing them in parallel to keep process dynamics the same. It implements a five-way splitter for process fluids to split the flows into five precisely divided streams for five-column cavities. This reduces the cycle time by one-fifth.

Similarly, fluids exiting from the five columns are collected into a chamber cavity and sent forward for further analysis. A thoroughly tested actuated valve block ensures precise flow patterns into column cavities. An advantage of this small-scale processing is that it ensures low buffer/water consumption/feed consumption in turn. RRAS overcomes the limitations of conventional resin aging studies because it is scaled down to dynamically simulate large-scale systems by enabling input flows through micro-resin wells. This provides the user with a realistic idea of industrial-scale resin performance.

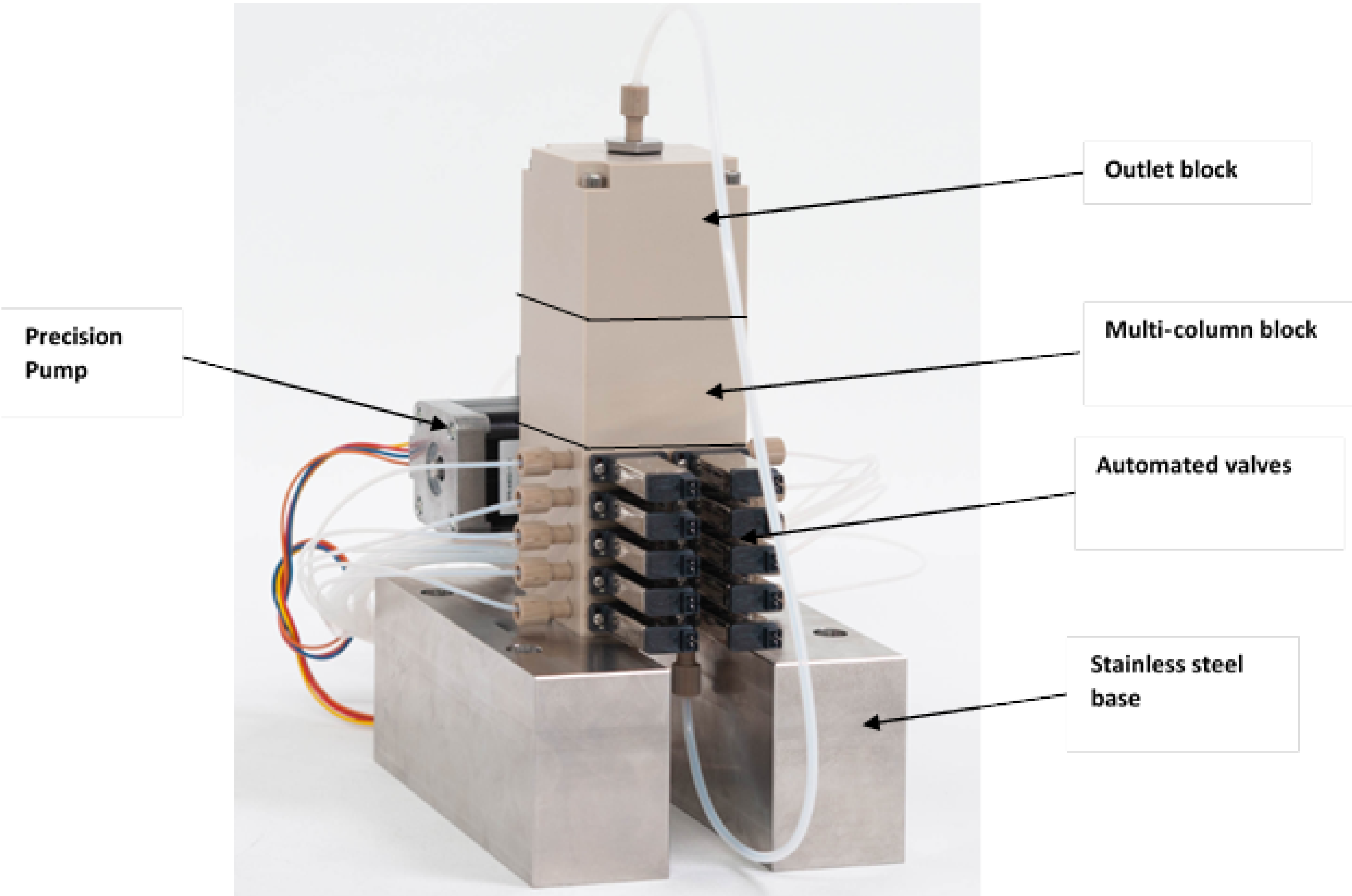

Figure 1. XPure-R Rapid Resin Aging System (RRAS)

Highlights of RRAS are described below:

- System is easy to install, use, and maintain, with flexibility for both packed and expanded bed adsorption (processing unclarified fermentation broth).
- Robust and reliable scale-down model for high throughput resin analysis with column volumes as low as 0.5 ml and flowrates between 0.01-2.5 ml/s.

- Customizable with broad selection of design modification and construction materials with the ability to test multiple scenarios at the same time.
- Flexible processing limits up to 10 barg and 90^{O}C, enabling testing of a wide range of resins (up to 40 Q particle size).
- Automated platform that requires minimal staff and ensures completely computerized execution of hundreds of cycles with desired precision.
- Includes a comprehensive software package running on Windows, enabling the user to perform experiments in an easy and automated manner, both manually and recipe-based.
- Built-in conductivity, pH, and UV sensors at the outlet capture the generated process and analytical data while a dashboard screen provides a current snapshot during any given point during the process.
- RRAS also comes with a fraction collector, enabling effortless sampling for further analysis.

Case Study

For an amino acid production process, a resin-aging study was performed. A column of 1 ml volume for each cavity, totaling up to 5 ml was filled with 0.5 ml resin per cavity and the resin was tested in the RRAS to check the performance in expanded bed adsorption (EBA) mode by pumping unclarified fermentation broth as feed-in up-flow for several hundred cycles. Processing steps such as feed, wash, elution, regeneration, and wash were run sequentially onto the resin using actual process parameters. Resin studies were performed continuously for approximately 5 days to finish 1,000 cycles. Without RRAS, the estimated time to perform the testing would have required a minimum of 50-60 days. Dynamic binding capacity for each cycle was plotted against the number of cycles to assess the resin performance. Figure 2 shows that the resin consistently performed well throughout the 1,000 cycles with no decline in the binding. The purity and yields were also found to be consistent and at par the desired criteria for all 1,000 cycles (data not shown here). This shows how RRAS can build confidence in the process and help users make key decisions with minimal time.

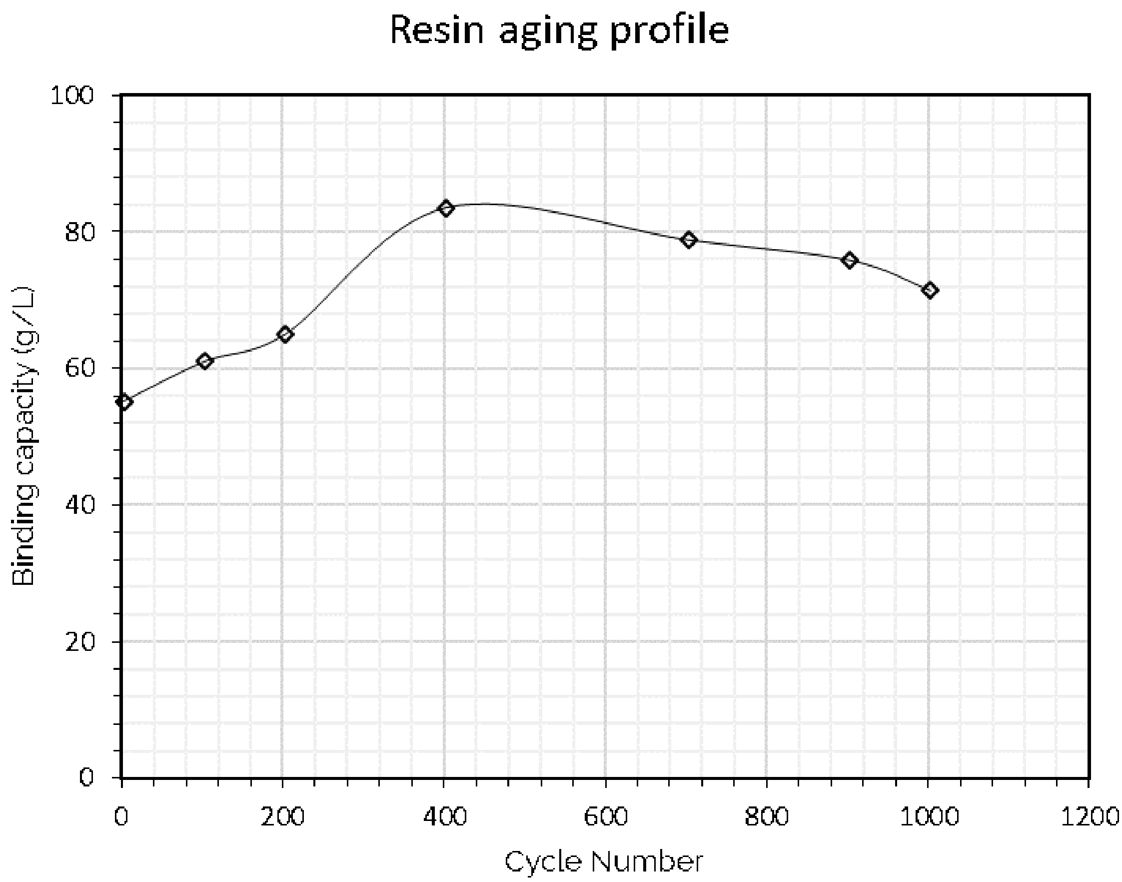

Figure 2. This graph shows that the resin consistently performed well throughout the 1,000 cycles with no decline in the binding. The purity and yields were also found to be consistent and at par the desired criteria for all 1,000 cycles (data not shown here). This shows how RRAS can build confidence in the process and help users make key decisions with minimal time.

Conclusion

With the advent of specialized chromatography techniques, different types of resins/adsorbents are being introduced in the market. With such a wide database of resins, it is very important to make the right choice using careful screening procedures. Resin screening based on separation efficiency alone cannot guarantee long-term performance because it does not factor in the variability of the resin characteristics with time allowed for sustainable performance. This suggests that in order to ensure optimal quality and economics of the process, resin screening should be followed by resin aging studies before finalizing the resin for scale-up and manufacturing.

Current methods of studying resin performance over time are cumbersome, time-consuming, and require ample resources. XPure RRAS provides an easy-to-implement, automated, and accurate platform to perform the resin studies. It reduces time-of-aging studies substantially due to parallel processing. Because RRAS, uses a highly customizable and flexible build, it provides options for carrying different studies at the same time while producing data for detailed analysis.

Today, faster process development approaches are crucial for rapid lab to market transitions, RRAS can be a reliable stepping stone to build the foundation of a successful product enterprise.

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