Technical Note: PuraBead® Resins

The manufacture of biological products using process chromatography was introduced over 50 years ago when ion exchange resins were first used at large scale for insulin production.

The foundations of Astrea Bioseparations' chromatographic resin technology lies in its proprietary PuraBead® base matrix, developed over 25 years ago to address industry challenges associated with processing biotherapeutic products, particularly plasma proteins. PuraBead® P6 is a near-monodisperse, 6% beaded agarose support which serves as the primary platform for attachment of Astrea Bioseparations' ligands. The unique properties of PuraBead® agarose beads have enabled it to become the resin of choice for a wide variety of applications from monoclonal antibodies to cell and gene therapies.

Why Agarose?

Today many chromatography resins are manufactured from microplastics such as polymethacrylate or polystyrene which require managed disposal so as not to enter and contaminate the environment, which further increases their overall cost of use. As we all become more aware of our environmental impact, it is critical to ensure green, sustainable choices are made whenever possible. In contrast to synthetic resins, PuraBead® has been developed from agarose, a natural polysaccharide extracted from certain species of marine algae (seaweed). It is a non-toxic, non-animal derived polymer, manufactured using highly controlled and ecofriendly techniques. A sustainable choice over synthetic resin beads.

Agarose is an ideal base matrix for chromatography resins due to being inert and naturally hydrophilic which reduces non-specific binding. This low binding characteristic ensures that only the ligands interact with the target, maximizing purity and minimizing product losses. While unreactive under normal use conditions, the abundance of hydroxyl groups allows ligand derivatisation using a wide range of chemistries.

After crosslinking, agarose beads have the ideal combination of high porosity, high surface area and sufficient rigidity to support high flow rates. This combination of properties ensures high capacities and shorter processing times.

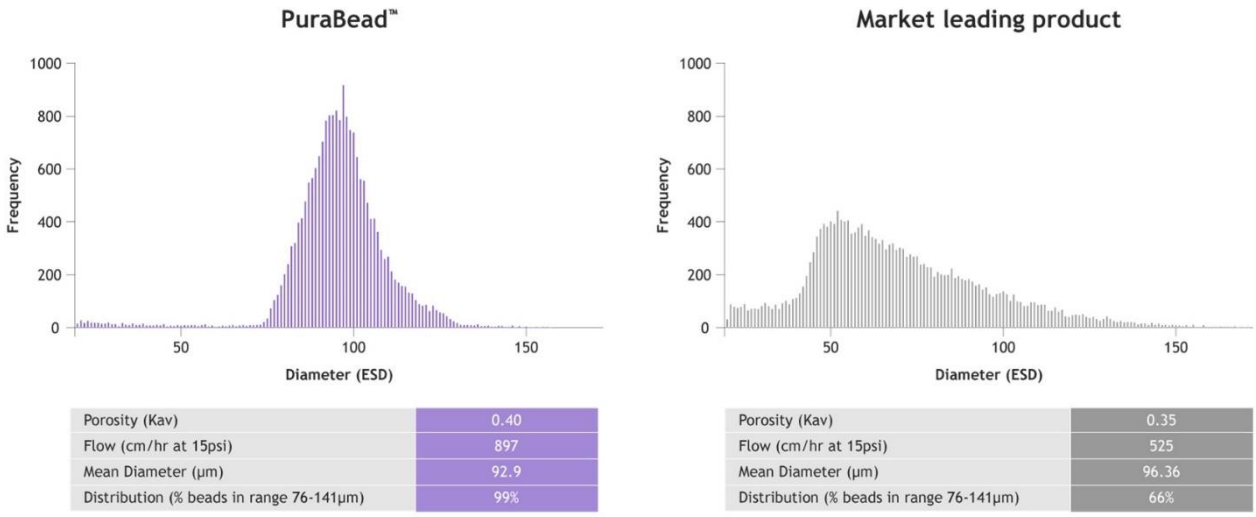
PuraBead® P6 resins

When manufacturing industry-leading chromatographic beads, selecting the highest quality materials is only part of the story. The manufacturing approach is also critical for product properties and performance.

Traditionally, agarose beads are produced by dispersing a hot aqueous solution of agarose polymer in a water immiscible solvent to emulsify the agarose solution. After cooling the agarose droplets gel to form agarose beads. This method results in large quantities of solvent waste that must be recycled or correctly disposed of, and the resulting beads require extensive washing to remove residual solvent. Additionally, this method creates a wide variation of bead sizes which affects performance when packed into a column, the smaller beads filling in the spaces between the larger beads, resulting in higher backpressures and irregular flow through the column.

Other methods have been developed to more closely control bead size, such as interrupting a stream of hot agarose solution as it passes through a sieve, a process known as jetting, to restrict the size of the beads that can form. However, like the emulsification process, this process also leads to high solvent consumption.

In contrast to traditional methods of producing agarose beads, Astrea Bioseparations utilizes a unique manufacturing method based upon the principles of spray atomization. Hot agarose solution is deposited onto a spinning disc to create a film layer. Controlling the film thickness/bead size is managed by adjusting the rotational speed of the disc and the rate of agarose solution addition to achieve optimal film thickness. At the edge of the disc the agarose film is ejected in the form of highly uniform droplets which cool and gel in air to produce almost monodisperse beads. In addition to a highly uniform bead size, this approach completely eliminates the need for solvents in the manufacturing process.



PuraBead™	
Porosity (Kav)	0.40
Flow (cm/hr at 15psi)	897
Mean Diameter (µm)	92.9
Distribution (% beads in range 76-141µm)	99%

Market leading product	
Porosity (Kav)	0.35
Flow (cm/hr at 15psi)	525
Mean Diameter (µm)	96.36
Distribution (% beads in range 76-141µm)	66%

Figure 1- Comparison of PuraBead® and other commercially available agarose beads

Why monodisperse beads?

PuraBead® resins have a highly uniform particle size distribution meaning the beads are all the same size and, when packed into a chromatography column, the spaces between adjacent beads (the liquid flow channels) are also all the same size. These features enable highly uniform packed columns with reduced flow resistance, higher operational flow rates and reduced column operating pressures. In-turn, this enables shorter processing times (particularly for larger volume columns with bed volumes >100 litres and/or longer bed lengths (>20 cm)) and increased resistance to blockage/fouling which maximises column lifetimes and avoids the need for frequent and costly column repacks.

The near-monodisperse nature of PuraBead® chromatography resins deliver reproducible and consistent performance allowing for easier and more consistent column packing and improved overall column performance.

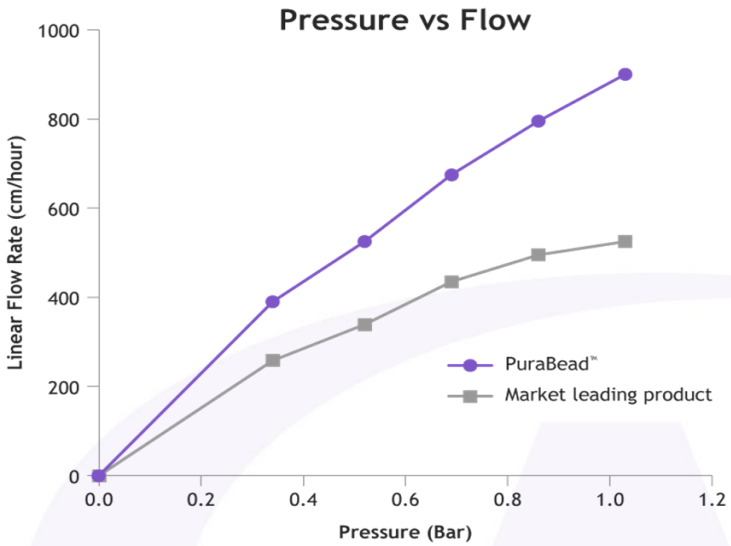


Figure 2 - Pressure vs Flow Comparison of PuraBead 6HF and a competitor product

New PuraBead® Edge

As biotherapeutic modalities become more specialized, chromatographic processes that reliably separate targets from impurities are in high demand by the industry. These evolving industry requirements necessitate the development of new resin beads with increased resolution and greater usable binding capacities. Both can be achieved by reducing the bead size. PuraBead® Edge, a newly developed 65 µm monodisperse beaded agarose support, meets these industry demands.

Utilizing smaller beads greatly increases binding capacity under dynamic flow conditions owing to the shorter diffusional path lengths in comparison to larger beads. The use of smaller beads also provides increased resolution, a critical feature when separating components by use of gradient elution. However, as bead size decreases, column back pressure increases which places limitations on maximum flow rates. To balance these competing parameters, Astrea Bioseparations has determined that 65 µm monodisperse beads provide the ideal balance of peak resolution and flow rate for maximal productivity.

Conclusion

The choice of which chromatography resin to incorporate into a workflow is affected by many factors, including base matrix, hydrophilicity, caustic stability, and consistency of bead size and shape, which all directly impact product performance. During times where sustainability and corporate responsibility are of growing importance, a product that exemplifies these needs without adversely affecting performance is highly desirable. PuraBead® chromatography resins manufactured at scale by Astrea Bioseparations are the ideal solution and offer a combination of caustic stability, high flow rates, low back-pressures and high capacities - in addition to the availability of different bead sizes to meet your separation requirements. Near-monodisperse bead sizing ensures consistent performance from batch to batch, whilst being sustainable and ecofriendly. By incorporating Astrea Bioseparations PuraBead® chromatographic resins into your biomanufacturing processes, you can be assured you are selecting the ideal resin for your target application.

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