potting adhesives for hollow fiber membranes

Biothane™ Polyurethane Systems in Biopharmaceutical Filters

The Role of Hollow Fiber Membranes in the Biopharmaceutical Value-Chain

The use of hollow fiber membranes (HFM) in the continuous production of biologics has long been established[1]. However, it was not until the pandemic afforded a rapid increase in investment and accelerated regulatory support that hollow fiber technology became a crucial part of the biotech industry's value chain, particularly for vaccine and viral vector manufacturing. The fast-evolving biomanufacturing landscape has created an opening for continuous bioprocessing, which is widely recognized as a next generation technology for reducing manufacturing cost, while providing more flexibility and scalability with improved product quality.

In the upstream operation of bioprocessing, where biotechnologists are constantly challenged to produce more cells and cell-products, HFM bioreactors have increasingly become popular[1,2] compared to conventional methods, such as T-flasks, roller-bottles and microcarriers. HFM Bioreactors offer many advantages such as the ability to produce high-density cells due to higher surface area-to-volume ratio, better cell viability due to a more in-vivo like culture environment, continuous harvesting and significantly smaller operational footprint.

In the downstream operation, continuous perfusion, tangential-flow HFM filter technology is commonly used to optimize filtration, maximize yield and achieve the desired quality attributes.

Potting Adhesive - A Critical Component of a Hollow Fiber Membrane Module

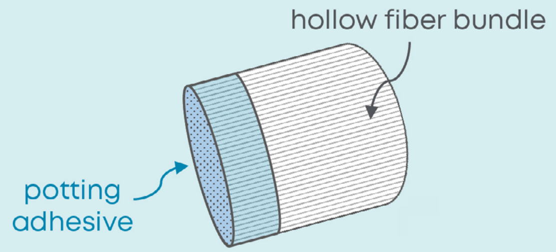
In a typical HFM biomanufacturing operation, the membrane helps separate and purify the cell concentrate, or acts as nucleation sites for culture growth. While much has been written about the membrane materials and selection criteria, a critical component often overlooked is the potting material that helps seal the membrane bundle together.

Though multiple materials have been investigated,[3,4] including silicone elastomers and epoxy resins, today 2-part polyurethane remains the material of choice for medical and biomedical applications. Other than providing the vital, reliable barrier between the retentate and permeate sides, this potting material must also survive the many stressors of the HFM operation for an optimized, efficient operation and a high-quality output:

- ***Biocompatibility*** to ensure safe interaction with system components and cell concentrate
- ***Broad pH compatibility*** to accommodate exposure to buffer solutions with pH ranges of 2-14 without experiencing changes in physical properties or leaching into the cell concentrate
- ***Chemical resistance*** to survive the multiple cleaning cycles, typically using NaOH solution, between batches to prevent fouling due to pore blockage
- ***Compatibility with various sterilization methods*** deployed to necessitate reuse of the filter, most commonly autoclave and gamma sterilization

application requirements

adhesion	biocompatibility
sterilizability	chemical resistance



potting performance

composition	process window
chemical stability	thermal stability

Biothane Polyurethane Systems provide a wide range of process and performance advantages for bio-filter applications.

Biothane™ Systems - A Biocompatible Solution for Biopharmaceutical Filters

Each Biothane System consists of two liquid components - the Vorite™ Prepolymer and the Polycin™ Polyol, which when mixed together cure at room temperature to yield a cross-linked polyurethane. Once combined, adhesive viscosity begins to increase as the chemical reaction develops a cross-linked network. As time progresses, the potting adhesive cures into a solid.

In the design of an HFM bioreactor and perfusion filter module, selection of a suitable filter cartridge potting adhesive starts with consideration of the type of membrane fiber being potted, primarily defined by the filtration requirements (micro-, ultra-, or nano-) and corresponding pore size. Full permeation of the membrane is achieved by leveraging the relationship between pore size and mix viscosity. The viscosity must be low enough for the adhesive to completely penetrate the spaces between fibers during the potting process, however excessively low viscosity can lead to clogging of pores.

Centrifugal and static potting processes require different potting adhesive viscosity profiles to set the membrane in the cartridge housing. An adhesive that increases in viscosity too quickly may result in defects such as bubbles or incomplete fill. Similarly, the rate of hardness development as the adhesive cures is an important factor in optimization of the cutting process. Filter cartridge cutting efficiency is guided by potting hardness and the rate at which it develops, relying on a tight window of hardness to enable clean cuts that properly open the membrane lumen while producing the necessary strength and adhesion for cartridge integrity.

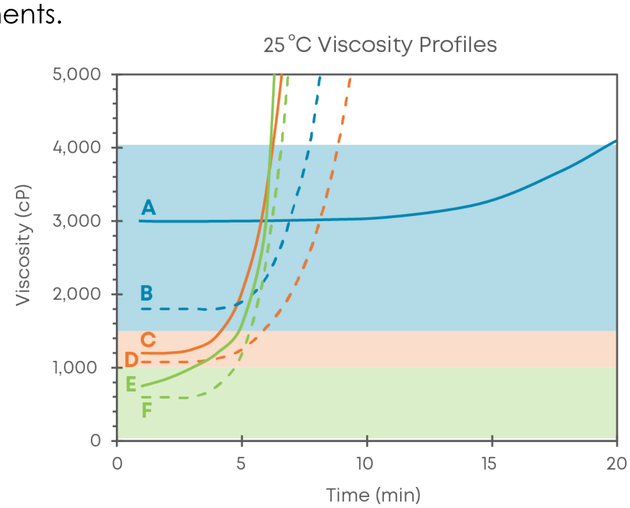
The Biothane System Advantage

- Biothane Polyurethanes have been specified as potting adhesives in critical biomedical applications since 1975
- These systems are specially formulated to meet the rigorous demands of various hollow fiber membrane applications such as dialyzers, oxygenators, and pharmaceutical filters
- Biocompatibility per ISO 10993
- Sterilizable via standard methods
- No significant change in physical properties following 24-hour soak in aqueous pH 3 or pH 12 solution
- Inherently hydrophobic chemistry
- Primarily derived from castor oil, a natural material
- Modular technology that can be tailored to suit assembly processes

The modular technology of these two-part Biothane Systems enables **Aurorium** to offer a broad spectrum of adhesive performance and physical properties required for a variety of upstream and downstream processes. Viscosity profiles in the figure below represent the spectrum of reactivity that can be achieved with various combinations of Polycin Polyol and Vorite Prepolymer components.

Filter Type	**Micro**		**Ultra**		**Nano**	
Membrane Pore Size (µm)	0.2 – 0.5		0.005 – 0.1		0.0001 – 0.001	
Biothane System	**A**	**B**	**C**	**D**	**E**	**F**
Vorite Prepolymer	689	689	2021	1752	2050	2050
Polycin Polyol	940-M4	1964	1964	2566	2566	1964
Process Properties						
Mix Viscosity*, 25°C (cP)	3000	1800	1200	1100	750	720
Gel Time, 25°C (min)	50	12	10	15	9	8
Physical Properties**						
Hardness (Shore D)	66	70	70	50	67	72
Tensile Strength (psi)	3300	3900	3600	3200	3700	3900
Elongation (%)	115	130	115	165	155	135

** Brookfield LVT viscometer measurement*
*** Physical properties measured after 60°C post-cure*



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