Crossflow Membrane Filtration of Biological Suspensions for Protein Recovery

by

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ABSTRACT

Biological molecules like proteins, monoclonal antibodies, peptides etc., form a large proportion of therapeutics in the product pipelines of firms in the biopharmaceutical industry. Since these molecules address major unmet medical needs, their timely clinical and commercial supply is critical. Pressure-driven membrane filtration processes, like microfiltration (MF) and ultrafiltration (UF), are widely used in the downstream concentration and recovery of protein therapeutics. This research aims to improve understanding of the factors important for both protein concentration and recovery. One part of the research involved the use of MF in the recovery of recombinant inclusion bodies, produced intracellularly in *E.coli,* while the other part concerned the recovery of precipitates of immunoglobulins at high yield and purity from bovine serum. Parametric studies were performed by varying flow rate, concentration of solids in the feed, physicochemical conditions like feed pH and ionic strength, and membrane pore-size to characterize the system. The actual separation was then performed through an optimized combination of batch concentration and diafiltration to obtain greater than 90 % yields and purity.

A high throughput technique for membrane surface modification and screening was tested to aid in the development of membrane surfaces to minimize protein adsorption in the presence of high salt. Binary mixtures of IgG (insoluble precipitate) and BSA (soluble) were used as feed challenge and surfaces were selected (from a library of 66 monomers) based on their ability to maintain selectivity for separation and reduce fouling (measured by lower fouling resistance). This work helps in addressing an unmet need in the rapid identification and design of membrane surfaces for protein filtration applications.

Finally, optimization maps were developed to aid in the accelerated process development of membrane-based microfiltration. A strategy was developed to meet the twin objectives of protein yield and processing time by incorporating the effect of parameters like sieving coefficient, concentration factor and diavolumes. This addresses an important need in the rapid optimization of MF processes.