Purification of monoclonal antibody by Membrane Assisted Crystallization

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Protein-based therapeutics, especially monoclonal antibodies (mAbs), are a large growing class of drugs in a continuous development and represent an integrated part of treatment of life-threatening conditions including cancer, autoimmune disorders, inflammatory, cardiovascular, respiratory, and infectious diseases[1]. However, the separation and purification of these therapeutics mainly based on expensive, time-consuming chromatographic methods represent a bottleneck in their production in the biopharmaceutical industry[2].
The challenge of current pharmaceutical research is to find alternative procedures able to replace conventional chromatography. Protein crystallization has long been applied to many industrial biomanufacturing processes in batch-mode and represents a cost-effective method to achieve high purity drug product. Nevertheless, this technique is far from being considered a technique of choice for the industrial purification of proteins due to its limitation regarding the scaling-up issue, the slow crystallization kinetics and the possible contamination that could affect the crystallization process[3].

This work aims to overcome these limitations adopting membrane-assisted crystallization technology in a continuous mode to achieve comparable yield and purity of the conventional chromatographic method but at more affordable cost and with high process efficiency. In particular, the continuous membrane crystallization concept has the ambitious goal of revolutionizing the current processes of industrial production of monoclonal antibodies thanks to the creation of membrane crystallizers operating continuously, able to separate and purify biological macromolecules directly in their clarified culture broth[3].
We investigated on the feasibility to crystallize a multi-component solution containing the mAb Anti-cluster of differentiation 20 (anti-CD20) concentrating it by solvent removal over a porous membrane to the vapour phase that allow to precisely control the concentration, and thus the generation of supersaturation during the crystallization process.
The main target of the work was to find appropriate operational conditions able to make the process compatible with the complex multi-component solutions tested. In fact, the crystallization solutions have increasing purity levels, starting from a preliminary mAb solution of high purity to a complex solution directly from clarified fermentation broth.
The efficiency of the final membranes was estimated in terms of mAb productivity, trans-membrane flux and rejection ability.

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