DESIGN OF A PERIODIC COUNTER-CURRENT CHROMATOGRAPHY PROCESS FOR EFFICIENT ONCOLYTIC VIRUS PURIFICATION

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Virus-based biologicals are one of the most promising biopharmaceuticals of the 21st century medicine and play a significant role in the development of innovative therapeutic, prophylactic and clinical applications. These biologicals share between them a high degree of complexity and offer various challenges requiring innovative technologies for their manufacturing. Oncolytic virus manufacturing scale can range from 5L in research and development up to 50L for clinical studies and reach hundreds of liters for commercial scale. The inehrent productivity and high integration potential of periodic counter-current chromatography offers a transversal solution to decrease equipment footprint and the reduction of several non-value-added unit operations.

The work to be reported focus on the design of a periodic counter-current chromatography process applied to the intermediate purification of oncolytic adenovirus. Moving away from single-column batch operation towards continuous or semi-continuous, multi-column chromatography creates the opportunity to benefit from synergies of solvent gradients, recycling chromatography, and simulated counter-current movement of the adsorbent and fluid phases, providing substantial reductions in chromatographic resin volume and buffer consumption. The developed ion exchange chromatographic purification method was carried out using a four-column setup, supported by mechanistic mathematical modeling. Obtained virus recoveries (> 60%) and impurity reductions (> 80% DNA, and > 70% total protein) match or overcome batch purification.

The impact of column cycling on column capacity will be presented and the steps taken to minimize it will be discussed, highlighting the optimization of the cleaning-in-place step and the need to include organic solvents to promote the stripping of tighter-adsorbing impurities. Moreover, the robustness of the dynamic control strategy and its ability to overcome perturbations originated in precedent stages will be demonstrated using feeds with different impurity profiles and titers, showing that it is possible to generate elution pools with consistent quality and traceability. Additionally, due to the wealth of data generated through the cycling operations, such as historic columns breakthrough and elution peak profiles, a deeper insight on product quality and process knowledge is gained. Moreover, process automation enables the minimization of errors, maximizing process efficiency, uptime, repeatability, and process replication.