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# Purification of a hepatitis C vaccine candidate: Comparison between multi- column chromatographic processes operated in positive and negative mode

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# PURIFICATION OF A HEPATITIS C VACCINE CANDIDATE: COMPARISON BETWEEN MULTI-COLUMN CHROMATOGRAPHIC PROCESSES OPERATED IN POSITIVE AND NEGATIVE MODE

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Given the increasing efficiencies in bioreaction and growing interest on complex biopharmaceutical products such as virus-like particles (VLPs), downstream processing (DSP) is becoming ever more relevant. Therefore, the biopharmaceutical industry is looking for alternative downstream strategies capable of improving purification yields whilst improving product quality and lowering costs. One of most promising improvements to DSP is to replace single-column batch operation by continuous, or semi-continuous, multi-column chromatography.

We report on the development and comparison of two types of multi-column chromatographic systems aimed at the purification of Hepatitis C VLPs, produced using insect cell-based expression with recombinant baculovirus. The first process described herein is based on direct product capture using an anion exchange chromatographic media and subsequent elution with the modulation of ionic strength. By using a multi-column approach, one is able to overcome the limits of dynamic binding capacity characteristic of single-column batch processes, thus increasing the media capacity utilization. The second process reported is based on negative chromatographic purification. In this approach elution conditions are such that impurities should adsorb on the chromatographic media whereas the product of interest flows through the column. Both process approaches are subjected to a temporal arrangement of operations steps suchlike column equilibration, product application, production and regeneration. Volumetric productivity thus depends not only on the optimal scheduling of the referred steps, but also upon factors such as media capacity for the product and related impurities, operational flow-rates, and mechanical limitations of the systems used.

The proposed analysis compares volumetric productivity, resin capacity utilization, equipment footprint and skid complexity for both purification strategies. Also we will demonstrate that the optimal design is a balance between the manufacturing scale, complexity and imposed product quality requirements.