IMPROVING DOWNSTREAM PROCESSING OF ENVELOPED VIRUS-LIKE PARTICLES WITH MULTI-COLUMN CHROMATOGRAPHY

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The interest in continuous downstream purification processes is rapidly growing as industry pursues the establishment of continuous manufacturing. Continuous multi-column chromatography is therefore looked as an enabling technology, capable of improving purification yields whilst improving product quality and lowering costs.

We report on the development and comparison of two types of multi-column chromatographic systems aimed at the purification of enveloped VLPs, produced using insect cell-based expression with recombinant baculovirus. By subjecting an array of chromatographic devices to a temporal sequence of operations steps, suchlike column equilibration, product application, production and regeneration, one is able to overcome the limits of dynamic binding capacity characteristic of single-column batch processes. This will enable the increase of volumetric productivity, column capacity utilization and subsequently a decrease on processing costs.

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. 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.

The proposed strategies will be compared in terms of their volumetric productivity, resin capacity utilization, equipment footprint and skid complexity. We will also demonstrate that the optimal design is not only a balance between the manufacturing scale, complexity and imposed product quality requirements, but depends also upon factors such as media capacity for the product and related impurities, operational flow-rates, and mechanical limitations of the systems used.