MULTI-COLUMN CHROMATOGRAPHIC PURIFICATION OF INFLUENZA VIRUS-LIKE PARTICLES

Sofia Carvalho, iBET/ITQB-UNL
sofiacarvalho@ibet.pt
Ricardo Silva, iBET
Cristina Peixoto, iBET/ITQB-UNL
Paula Alves, iBET/ITQB-UNL
Manuel Carrondo, iBET/FCT-UNL

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Seasonal Influenza occurs all over the world and causes approximately 500 million cases of infection and up to 500 thousand deaths annually. The most effective way to prevent the disease is throughout vaccination. However, the constant antigenic drift on the influenza virus implies an annually vaccine update with high inherent costs. A new generation of virus-like particles (VLPs) vaccines, that have the ability to stimulate the production of broad antibody response to different Influenza strains, is a promising approach to solve this problem. VLPs have become a promising solution for influenza pandemics as well. The high attractiveness of VLPs has led to an increasing interest in the development of VLP purification processes as it often accounts for the major production costs. Therefore, it is mandatory to improve downstream processing (DSP) trains, not only to increase the efficiency of the existing processes but also to develop new unit operations capable of coping with the stringent regulatory requirements.

One of the most promising improvements to DSP is to replace single-column batch operation by continuous, or semi-continuous, multi-column chromatography. The process herein described is based on the optimal scheduling of the operations steps characteristic of a single-column bind and elute operation such as equilibration, product application, production and regeneration applied to a train of two columns. In fact, a simple serial connection of two columns, during the product application step, directing the effluent of the first column in the train to an adjacent one, allows the capture of the mass transfer zone. This setup modification not only avoids product loss but also greatly increases the capacity utilization of the chromatographic media by achieving column saturation.

We report on the development of a multi-column chromatographic process aimed at the purification of influenza VLPs, produced using insect cell-based expression with recombinant baculovirus. The inherent potential to improve process efficiency and economics, providing a powerful and flexible alternative to conventional batch chromatography will be demonstrated highlighting the impact of factors such as manufacturing scale, the complexity of the experimental setup and imposed product quality requirements.