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PII: S1570-0232(18)30879-1
DOI: doi:10.1016/j.jchromb.2018.08.014
Reference: CHROMB 21330

To appear in: *Journal of Chromatography B*

Received date: 2 June 2018
Revised date: 7 July 2018
Accepted date: 19 August 2018

Please cite this article as: Mohsen Bagheri, Hamid Reza Norouzi, Seyed Mohammad Javad Hossienizadeh, Ali Es-haghi, Alireza Ghassempour , Development and modeling of two-dimensional fast protein liquid chromatography for producing nonstructural protein-free food-and-mouth diseases virus vaccine. Chromb (2018), doi:10.1016/j.jchromb.2018.08.014

Development and Modeling of Two-Dimensional Fast Protein Liquid Chromatography for Producing Nonstructural Protein-free Food-and-Mouth Diseases Virus Vaccine

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Abstract

Concerns for the use of non-purified or incompletely purified inactivated foot-and-mouth disease (FMD) vaccine, like difficulties for differentiation vaccinated from infected animals, can be a motivation in order to develop methods based on size exclusion chromatography (SEC). In this study, a two dimensional size exclusion chromatography (2D-SEC) system has successfully constructed using two different SEC column media to achieve a high-throughput purification system for the cell culture-derived foot and mouth diseases virus (FMDV). A mathematical model has also utilized to predict and get a better insight into the separation process. Column and the packing particles characteristics consisting of column void volume, total column volume, particle porosity and accessible particle porosity have acquired experimentally. Retention times and elution profile of two different molecules, blue dextran and bovine serum albumin, were used for evaluating the capability of SEC media for separating two critical impurities (residual DNA (rDNA) and non-structural protein (NSP)) from active ingredient of vaccine (FMDV particle). Experiments were carried out with two different commercial columns (XK 26/60) and (XK 16/100) and with four different packing media superdex 200 prep grade, sephacryl S-500 HR, Sephacryl S-400 HR and Sephacryl S-300HR. The mathematical model was first validated by experimental chromatographic data of different SEC media and then was used to propose the best 2D-SEC system for downstream processing of the FMDV vaccine. The loading capacity of the constructed 2D-SEC sample was increased to 12.5% of total column volume and the purity of the final product was more than 90%. The entire purification process was performed with 77% FMDV recovery and 79.1% virus yield. Based on the high-performance size exclusion chromatography (HPSEC), the purity of the final NSP-free FMDV was about 90% and over 94.6% of host cell DNA was removed.