

## Accepted Manuscript

Title: An Integrated Precipitation and Ion-exchange Chromatography Process for Antibody Manufacturing: Process Development Strategy and Continuous Chromatography Exploration

Author: Steffen Großhans Gang Wang Christian Fischer  
Jürgen Hubbuch

PII: S0021-9673(17)31773-9  
DOI: <https://doi.org/doi:10.1016/j.chroma.2017.12.013>  
Reference: CHROMA 359069

To appear in: *Journal of Chromatography A*

Received date: 16-10-2017  
Revised date: 4-12-2017  
Accepted date: 5-12-2017

Please cite this article as: Steffen Grosshans, Gang Wang, Christian Fischer, Jddoturgen Hubbuch, An Integrated Precipitation and Ion-exchange Chromatography Process for Antibody Manufacturing: Process Development Strategy and Continuous Chromatography Exploration, <![CDATA[*Journal of Chromatography A*]]> (2017), <https://doi.org/10.1016/j.chroma.2017.12.013>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



# An Integrated Precipitation and Ion-exchange Chromatography Process for Antibody Manufacturing: Process Development Strategy and Continuous Chromatography Exploration

Steffen Großhans\*, Gang Wang\*, Christian Fischer, Jürgen Hubbuch\*\*

*Karlsruhe Institute of Technology (KIT), Institute of Process Engineering in Life Sciences, Section IV:  
Biomolecular Separation Engineering, Karlsruhe, Germany*

## Abstract

In the past decades, research was carried out to find cost-efficient alternatives to Protein A chromatography as a capture step in monoclonal antibody (mAb) purification processes. In this work, polyethylene glycol (PEG) precipitation has shown promising results in the case of mAb yield and purity. Especially with respect to continuous processing, PEG precipitation has many advantages, like low cost of goods, simple setup, easy scalability, and the option to handle perfusion reactors.

Nevertheless, replacing Protein A has the disadvantage of renouncing a platform unit operation as well. Furthermore, PEG precipitation is not capable of reducing high molecular weight impurities (HMW) like aggregates or DNA. To overcome these challenges, an integrated process strategy combining PEG precipitation with cation-exchange chromatography (CEX) for purification of a mAb is presented.

This work discusses the process strategy as well as the associated fast, easy, and material-saving process development platform. These were implemented through the combination of high-throughput methods with empirical and mechanistic modeling. The strategy allows the development of a common batch process. Additionally, it is feasible to develop a continuous process. In the presented case study, a mAb provided from cell culture fluid (HCCF) was purified. The precipitation and resolubilisation conditions as well as the chromatography method were optimized, and the mutual influence of all steps was investigated. A mAb yield of over 95.0 % and a host cell protein (HCP) reduction of over 99.0 % could be shown. At the same time, the aggregate level was reduced from 3.12 % to 1.20 % and the DNA level was reduced by five orders of magnitude. Furthermore, the mAb was concentrated three times to a final concentration of 11.9 mg/mL.

**Keywords:** Antibody manufacturing, Integrated processing, Protein precipitation, Mechanistic modeling, Periodic counter-current chromatography

\*These authors contributed equally to this work.

\*\*Corresponding author

E-mail address: juergen.hubbuch@kit.edu

Telephone: +49 721 608 47526

Preprint submitted to Journal of Chromatography A

Download English Version:

<https://daneshyari.com/en/article/7609080>

Download Persian Version:

<https://daneshyari.com/article/7609080>

[Daneshyari.com](https://daneshyari.com)