Prediction models for the flux decay profile and initial flux of microfiltration for therapeutic proteins

Susumu Uchiyama[1], Kota Inoue[2], Yumiko Masuda[2], Tetsuo Torisu[1], and Koichi Nonaka[2]

[1]Osaka Daigaku Kogakubu Daigakuin Kogaku Kenkyuka
[2]Daiichi Sankyo Kabushiki Kaisha

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Abstract

Microfiltration is an essential step during biopharmaceutical manufacturing. However, unexpected flux decay can occur. Although the flux decay profile and initial flux are important factors determining microfiltration filterability, predicting them accurately is challenging since the root cause of unexpected flux decay remains elusive. In this study, the methodology for developing a prediction model of flux decay profiles was established. First, the filtration profiles of different monodisperse polystyrene latex and silica beads of various sizes were evaluated. These results revealed that the size and surface electrostatic properties of the beads affect the flux decay profile. Taking the size and surface electrostatic properties of protein aggregates into account, we constructed a predictive model using model bead filtration profiles. We showed that this methodology was applicable to two different microfiltration filters to predict the flux decay profile of therapeutic proteins. Since this prediction model is based on normalized flux, the initial flux must be predicted. We therefore successfully developed a method to predict initial flux based on the Hagen-Poiseuille equation using sample viscosity values for both filters. These prediction models can be used for effective microfiltration scale-up assessment and can be applied during early stage of process development.

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