PERIODIC COUNTER-CURRENT CHROMATOGRAPHY FOR CONTINUOUS PURIFICATION OF MONOCLONAL ANTIBODY

Ho-Lung Jiang, Development Center for Biotechnology, Taipei, Taiwan, Republic of China
bard@mail.dcb.org.tw
Yue-Chang Chou, Development Center for Biotechnology
San-Cher Chen, Development Center for Biotechnology
Ching-Jen Yang, Development Center for Biotechnology
I-Ling Kou, Development Center for Biotechnology
Wei-Kuang Chi, Development Center for Biotechnology

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Integrated and continuous processing of antibody drugs offers several advantages over traditional batch processing in the biotechnology industry. The flexibility of periodic counter-current (PCC) design is performed in the selection of residence time and column numbers on the capture process. In this study, we investigate the association of residence time and product recovery in the downstream PCC purification. A practical operation of PCC as a continuous capture purification step has been applied to 50L feed-bath culture, 5L perfusion culture and 5L concentrated feed-batch culture. Protein breakthrough curve was determined for the appropriate column switching strategy. Using an empirical model for the protein breakthrough curve, residence time (RT) was evaluated and the loading flow rate was adjusted to achieve a target RT of 2.25 minutes for monoclonal antibody (mAb). The sample load volume for each column switching was set on 50-58% breakthrough curves, mAb recovery was 83-92%, and buffer consumption was decreased to under half that of the batch process. Overall, 1.0 to 1.5 gram mAb was obtained for per milliliter resin in 24 hours using a PCC purification system. We used size exclusion-high performance liquid chromatography to confirm composition and masses of our fragment samples. Comparison of qualities of mAb analyzed by UPLC and reverse phase chromatography show that glycan profiles and purity are quite similar between PCC and Avant purification, whereas that for acidic variants are different, the acidic variants of mAb purified by PCC is higher than that purified by Avant. The advantages of a continuous downstream capture step are highlighted for our case study in comparison with the existing batch chromatography processes. The use of PCC improves the higher resin capacity utilization and lower buffer consumption.