Impurity removal by ion-exchange membrane absorbers

A fully continuous, downstream process represents one of the most interesting novel purification approaches in the biosimilars industry. This would enhance the production output while reducing the costs of complex biopharmaceuticals. Since it generally involves several chromatographic steps, the selection of appropriate chromatographic columns is of utmost importance. In this study we compared several commercially available ion-exchange-membrane adsorbers (NatriFlo®, Sartobind® and Mustang®). In the first part of the thesis, basic characterisation of the selected membrane adsorbers was performed, whereas in the second part of the thesis the removal of host cell proteins (HCPs) and monoclonal antibody aggregates in the flow-through mode was evaluated. Dynamic binding capacity, ionic capacity and type of ligand were determined for individual membrane adsorbers, using simple, fast and non-invasive methods. Design of Experiments (DoE) was employed to determine the optimal pH and conductivity conditions. We demonstrated that all the anion-exchange-membrane adsorbers were capable of removing HCPs from monoclonal antibody mixtures below the required threshold across a wide range of sample pHs and conductivity values, and that the HCPs' normalised outlet concentration increases almost linearly with loading, being independent of the HCPs' concentration. No significant differences in the profile of the adsorbed HCPs with respect to the membrane adsorbers were observed based on 2D electrophoresis analysis data, although they exhibited different binding capacities. Cation-exchange-membrane adsorbers were also tested for the removal of aggregates. The Yamamoto model was used to determine the number of binding sites and estimate the conductivity range for efficient removal of aggregates, while maintaining a high monoclonal antibody recovery. However, the obtained range had to be further fine-tuned experimentally, due to displacement phenomena. Differences in the trends of binding-site number with a change in the pH value for the tested cation-exchange adsorbers indicate slightly different adsorption mechanisms. To obtain optimal process performance, adjustments of the pH and conductivity were required between the anion- and cation-exchange steps.