SMALL-SCALE END-TO-END MAB PLATFORM WITH A CONTINUOUS AND INTEGRATED DESIGN

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Fully continuous manufacturing of therapeutic proteins is an emerging trend in the biopharmaceutical industry. Integration of the upstream and downstream processes and conversion to continuous manufacturing leads to increased productivities, decreased equipment size, improved product quality, and overall reduced production costs. An integrated continuous bioprocess (ICB) from the early stages of process development can accelerate the transfer of a new drug candidate to commercial manufacturing. The process presented in this work is a proof-of-concept of an end-to-end monoclonal antibody (mAb) production platform at small scale. It was implemented by a 200 mL ATF perfusion bioreactor, integrated with a single lab-scale chromatography system, performing all purification steps for the mAb from the cell culture harvest in a continuous way. The downstream process consisted of a periodic twin-column capture with protein A resin, followed by a virus inactivation step, a cation exchange step in bind-elute mode, and an anion exchange step in flow-through mode. MAbs were produced for 17 days in a high cell density perfusion culture of CHO cells and purified continuously with a recovery yield of up to 60 % by the following downstream train. A 5-log reduction of host cell protein levels revealed that impurities were sufficiently removed. A consistent glycosylation pattern of the purified product was ensured by the steady-state operation of the process. With this proof-of-concept, we demonstrated the technical feasibility of a fully continuous end-to-end process with a compact design, integrating several unit operations in a single chromatography station and using small-size equipment for the upstream and downstream operations. The work presented here can become a useful development tool for the future of continuous bioprocesses.