SOLID POLYETHYLENE GLYCOL PRECIPITATION: POTENTIAL COST REDUCTION IN ANTIBODY DOWNSTREAM PROCESSING

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A novel method for continuous precipitation of antibodies will be shown, where PEG is added as a solid to the supernatant. Precipitation becomes particularly interesting as an alternative to chromatography systems to capture recombinant antibodies, because it can be rendered into a truly continuous operation without interrupting the mass flow for the product. Precipitation can be easily adapted to work in a continuous mode using tubular reactors and scaled up. Precipitation is also insensitive to variations in feed concentrations as previously shown same reactor configurations could be used for a feed ranging from 0.5-8 g/l antibody in the supernatant. Economic analysis showed that precipitation-based processes reduce costs at all stages compared to protein A columns. In these CoGs studies, the main cost contribution of materials in precipitation were the use of large amounts of concentration stock solutions of precipitating agents and washing and resolubilization buffers. Protein precipitation is carried out by adding a stock solution of a precipitating agent to the supernatant to reach precipitation conditions. The addition of the stock solution increases the volume which must be processed in order to harvest and redissolve the precipitate and further purification, and thus, it increases equipment size and buffer consumption and consequently costs and the environmental footprint measured by the process mass intensity. Hence, the elevated buffer consumption is still an impediment to fully consider protein precipitation as an option to substitute chromatography systems. Another drawback of working with precipitating agents such as PEG6000 is that stock solutions need to be close to the maximal solubility. The preparation of such stock solutions requires long mixing times and a high viscosity is obtained. Since viscosity has a significant impact on the performance of the unit operations, the bioprocess design and economics needs to be adapted accordingly. Therefore, working at such PEG concentrations can be challenging and unfavourable. We developed a new strategy for PEG precipitation avoiding the preparation of stock solutions. PEG6000 in a powder form is directly fed into the clarified culture supernatant. The powder feeding device was connected to an Äkta purification system and combined with a tubular reactor, where the precipitation occurs. Protein precipitation was continuously performed over a duration of 4h. We obtained yields and purity as compared to conventional addition of 40 % PEG stock solution. Total cost of goods and the environmental footprint of the direct addition of solid PEG and addition of a 40% stock solution were compared. Solid PEG precipitation showed a remarkably reduction of buffer consumption and equipment size and significantly reduced the up to 35 % production costs. The reduction of water and working at more concentrated solutions also impacted the environmental footprint and process cost. The availability of such a process will increase significantly the scientific capacity and open new horizons on setting up innovative process ideas.