Separation of Protein Crystals in a Dynamic Cross-Flow Device

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Crystallization is a common technique for purifying and formulating proteins in the pharmaceutical industry. In particular, proteins with a high molecular weight, e.g. monoclonal antibodies, crystallize out in low concentrations due to the low solubility of the proteins. Furthermore, the crystal sizes reached are really small, and the solid density is low because of the high water content that can exceed 50%. These factors limit the selection for the solid-liquid separation process. One appropriate technique for separation of such particulate system is dynamic cross-flow filtration (DCF). In this special cross-flow apparatus, the tangential flow, which inhibits filter cake building, is caused by a stirrer that is positioned near the membrane. The filtration behavior hence is relatively independent of the particle size, and the suspension can be concentrated up to 70 Vol% solids content. However, stirring of the shear-susceptible protein crystals leads to attrition and/or breakage during the separation process. Firstly, this induces the formation of a fouling layer on the membrane. Due to the flow conditions during cross-flow processes, the risk of layer formation increases with a higher fraction of fines. This decreases the filtrate flow and hence causes a worse filtration performance. Secondly, the reduction of the crystal size worsens following product formulation steps.

For this reason, the magnitude of crystal breakage during concentration of the slurry in a DCF test apparatus manufactured by Bokela GmbH (Dynotest) and its influence on the separation performance are investigated in this work. The stirring speed is varied to find optimal separation conditions for the crystallized model protein lysozyme. The reduction of the crystal size depending on the stirring time and suspension concentration is discussed.

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