



acib

Austrian Centre of Industrial Biotechnology

Programme: COMET – Competence Centers for Excellent Technologies

Programme line: K2-Centres

COMET subproject, duration and type of project:

Continuous reactors for downstream processing, 10/2014 –12/2015, strategic project

Continuous Purification of Next-Generation Antibody Therapeutics

acib researchers have developed a novel purification method for continuous manufacturing of recombinant antibodies that can be used for the treatment of life-threatening diseases such as various cancers and inflammatory disorders. Continuous processes in general have shown to be advantageous compared to their batch counterparts used in industry today. The continuous unit operation developed at acib can help to streamline the manufacturing process of future antibody therapeutics, reduce their manufacturing costs significantly and thus expand their availability to non-privileged countries.



Success story

Antibodies for the treatment of life-threatening diseases such as cancer or inflammatory disorders are produced predominantly in mammalian cell culture today. Only about 20% of the total production costs of antibody therapeutics are caused by the actual production, while 80% of the costs are allocated to the subsequent purification in order to obtain the antibody in high enough purities for therapeutic uses. The purification process is usually operated in a batch wise mode, one purification step after the other.

It has been shown that a continuous process is more desirable as it stream-lines the purification process, is more cost effective and would yield more uniform product. Steady improvements in the cell lines used for the production of antibodies have resulted in high antibody concentrations. These concentrations can cause problems in the established purification processes. Here the new purification method comes into play. Researchers from the Austrian Centre of Industrial Biotechnology (acib) and the University of

Natural Resources and Life Sciences Vienna (BOKU) developed a novel purification method based on a series of simple, yet selective precipitation steps.

In a first step, impurities are precipitated by Calcium phosphate flocculation, followed by precipitation of the antibody product by cold ethanol. The novel method is ideally suited for the purification of high-titer feedstocks that are already encountered today and will become standard in the future. In a feasibility study, exemplified by the purification of an antibody provided by a large biopharmaceutical company, acib's method demonstrated to compete with the established purification method in terms of yield and exceeded with regard to speed of operation. A further advantage is, that the operation parameters needed for successful continuous operation can be optimized in a resource saving fashion in batch mode, thereby facilitating process development. The continuous process could be operated for extended periods of time without interruption or change in critical quality parameters. "Our method shows great potential as a

new platform technology for the pharmaceutical industry”, says Prof. Alois Jungbauer, who is in negotiations with several international companies about building pilot plants.



Fig. 1: Precipitate flocs of antibodies being produced continuously in a tubular reactor.

Impact and effects

From a technical point of view, the novel unit operation developed at acib can help to streamline production processes. Operated in continuous mode, intermediate, non-value adding hold steps can be omitted. Smaller equipment can be employed during continuous operation, because only small volumes are processed at any time. A high degree of automation reduces the risk for human error.

Based on the results achieved in this strategic project, a new industrial partner could be acquired, financing a follow-up project. In this

project, the concepts of precipitation will be applied for the purification of challenging non-antibody protein products.



Fig. 2: A custom-fabricated test reactor capable of rapid cooling used for the continuous cold ethanol precipitation of recombinant antibodies from cell culture fluids is maintained by acib researcher Nikolaus Hammerschmidt.

Contact and information

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Project partners

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