Microbial Cell Factories

Oral Presentation

Industrial scale production of chymosin with *Aspergillus niger*

Karsten Hellmuth*

Address: Department of Process Development, Ch. Hansen GmbH, Gr. Drakenburger Str. 93-97, D-31582 Nienburg, Germany
* Corresponding author

from The 4th Recombinant Protein Production Meeting: a comparative view on host physiology
Barcelona, Spain. 21–23 September 2006

Published: 10 October 2006

Microbial Cell Factories 2006, **5**(Suppl 1):S31 doi:10.1186/1475-2859-5-S1-S31

Background

Aspergillus niger has a long history as a producer of food-grade enzymes and is established as a GRAS (Generally Recognized As Safe) organism. As Chymosin has been created by nature to coagulate cow's milk, it is not surprising that chymosin is the most commonly used enzyme for cheesemaking. Since more than 10 years Chr. Hansen is producing chymosin by a large scale fermentation process.

Results

The genome of *A. niger* was modified by inserting a prochymosin c-DNA via an expression vector. Chymosin is secreted as a fusion protein with glucoamylase and processed to the active protein during fermentation. After cultivation the biomass is inactivated by lowering the pH-value and separated by filtration. For concentration and purification of chymosin a one-step EBA (Expanded Bed Adsorption) chromatography is used. This new production process is illustrated in Figure 1.

During the last years the fermentation process was optimised by changing various parameters like feeding strategy and inoculation procedure of the Seed fermentor. The concentration step with an aqueous two-phase system with PEG (poly-ethylen-glycol) and the purification step with an ion-exchange chromatography step were replaced by one-step EBA chromatography.

Conclusion

The simplified downstream process reduced the costs for waste water treatment and increased the recovery yield. Due to its high quality, the unlimited availability and its competitiveness to other milk clotting enzymes the market share of fermentation produced chymosin (FPC) increased significantly over the last years.

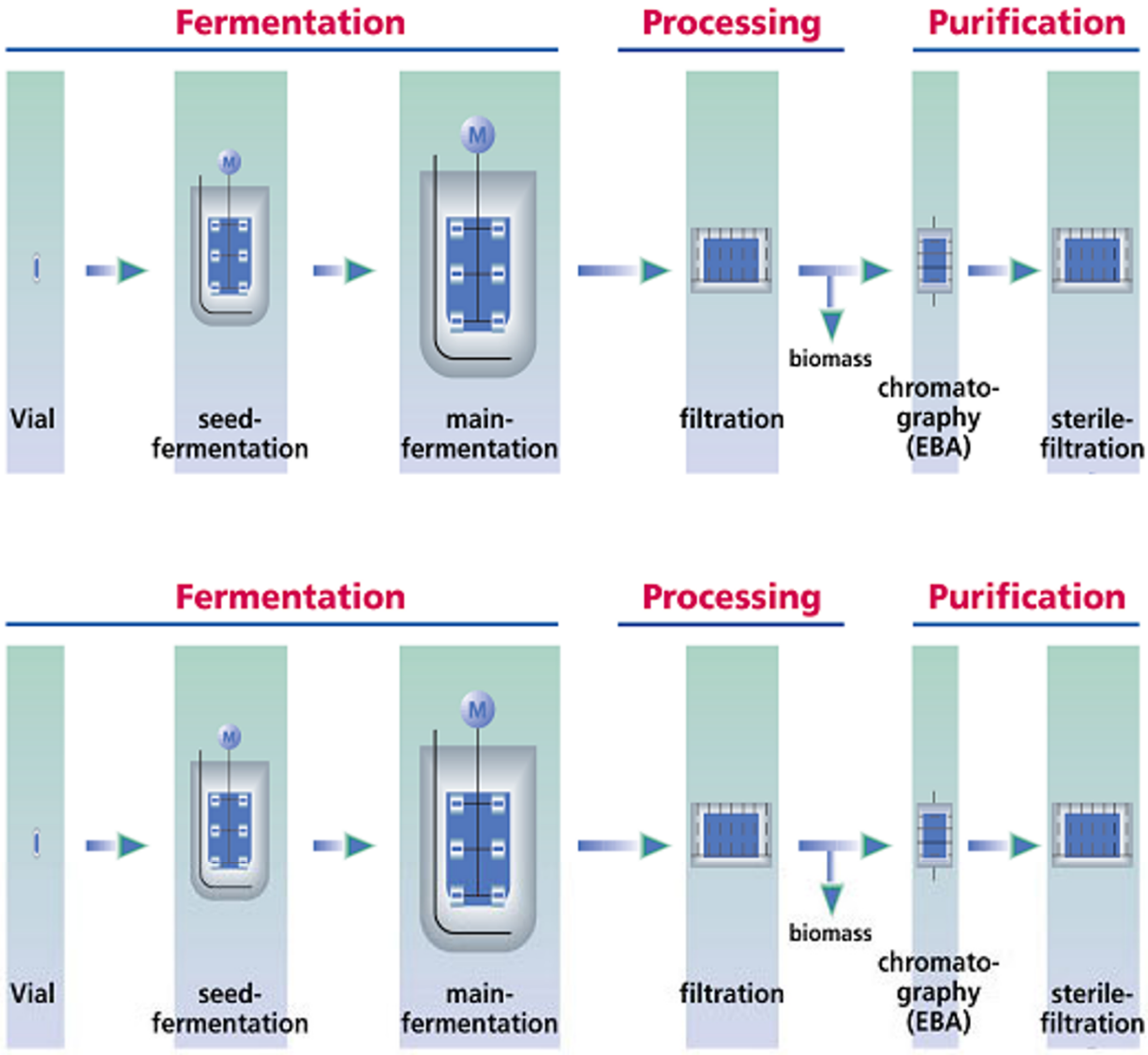

Figure 1
Chymosin production process; fermentation and downstream processing.