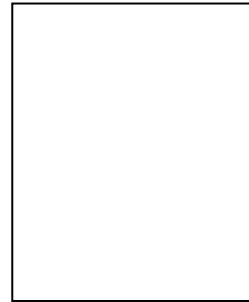


New process concepts for the enzymatic synthesis of amoxicillin from penicillin G

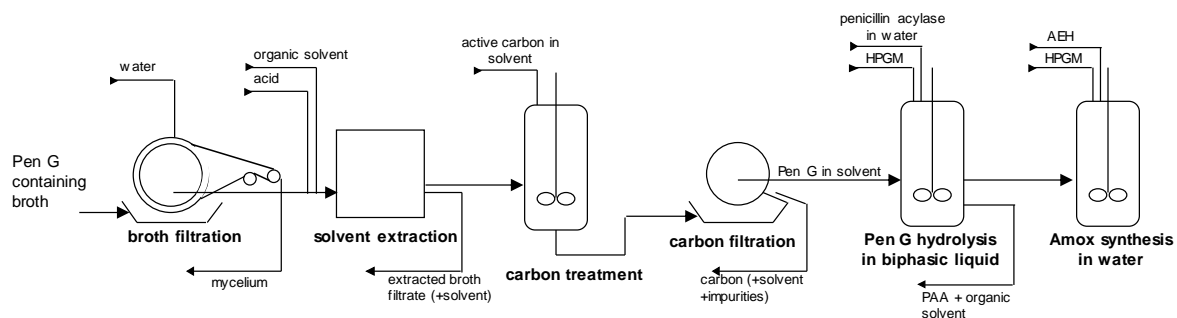
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Promotor: Prof.Dr. J.J. Heijnen
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Institute: Delft University of Technology, Department of Biotechnology
Project term: 1996 – 2000
Financed by: Chemferm, Ministry of Economic Affairs



Description

The aim of this work was to develop new enzymatic process concepts for the production of semisynthetic penicillins, with the emphasis on the enzymatic coupling reaction of 6-aminopenicillic acid (APA) and a side chain. It comprises the enzymatic coupling reaction of APA and a side chain, and possibilities for shortcut routes.

For example, we have studied the synthesis of amoxicillin in a suspension-to-suspension reaction without pH control. The pH is influenced by several pH-dependent (sub)processes such as the dissolution of the substrates, the coupling reaction and the undesired reactions. We have developed a model, which can describe the pH course of this reaction system. With this model, we were able to optimize the process conditions for the synthesis of amoxicillin. This model also gives a better understanding of all individual (sub)processes taking place.



Dissertation

M.B. Diender, New process concepts for the enzymatic synthesis of amoxicillin from penicillin G. PhD thesis, Delft University of Technology, 2001. <http://resolver.tudelft.nl/uuid:82309a92-ce45-42de-8cd2-e363609cbf47>

Publications from the dissertation

1. M.B. Diender, A.J.J. Straathof, L.A.M. van der Wielen, C. Ras and J.J. Heijnen, Feasibility of the thermodynamically controlled synthesis of amoxicillin. *J. Mol. Catal. B Enzym.*, **5** (1998) 249-253.
2. M.B. Diender, A.J.J. Straathof, and J.J. Heijnen, Predicting enzyme catalyzed reaction equilibria in cosolvent-water mixtures as a function of pH and solvent composition, *Biotransform.*, **16** (1998) 275-298.
3. M.B. Diender, A.J.J. Straathof, T. van der Does, M. Zomerdijk and J.J. Heijnen, Course of pH during the formation of amoxicillin by a suspension-to-suspension reaction. *Enzyme Microb. Technol.* **27** (2000) 576-582.

4. M.B. Diender, A.J.J. Straathof, T. van der Does, C. Ras and J.J. Heijnen, Equilibrium modelling of extractive enzymatic hydrolysis of penicillin G with concomitant 6-aminopenicillanic acid crystallisation. [Biotechnol. Bioeng. 78 \(2002\) 395-402.](#)
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