

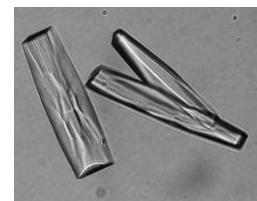
## Enzymatic synthesis and purification of semi-synthetic antibiotics in a counter-current reactor

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### Description

This work studies the enzymatic hydrolysis of penicillin G (PenG) into 6-aminopenicillanic acid (6-APA) and phenylacetic acid (PAA). In a multi-stage countercurrent reactor and at low pH, the enzymatic reaction takes place in the aqueous phase and the products are separated between the aqueous phase and organic phase (butyl acetate - BuAc). Furthermore, 6-APA crystallization occurs at low pH when PenG concentrations are high. Both phenomena shift the equilibrium towards conversion of substrate, favoring high productivity. The first step of this work, concerns the evaluation of activity and stability of penicillin amidase at low pH and in the presence of butyl acetate (BuAc). The enzyme presented the maximum activity in the pH 8.0 – 9.0 and remained stable at low pHs (3.0 – 6.0) during at least 32 days. Although the enzyme activity decreased by 80%, this does not represent a drawback in the application of a biphasic (water and BuAc) and continuous PenG hydrolysis at low pH. The effect of PenG, PAA and BuAc in APA crystallization and the kinetic parameters were also analyzed. The results showed that impurities have no effect on APA crystallization, in the pH range 4 – 5 and in the impurity concentrations of 0.55 – 3.0 mM. The evaluation of crystallization kinetics allowed the use of a model that predicts the APA crystallization rates. The data provided by the model can be used to optimize the operation conditions: stage of feed, flow rate of phases and initial substrate concentration. In the last step of this work, a literature review concerning extractive bioreactor was made.



### Dissertation

J.S. Ferreira, Processo intensificado de hidrólise de penicilina g e purificação dos produtos em reator multi-estágio e contra-corrente (Portuguese/English). PhD Thesis, UNICAMP, 1994.

### Publications from the dissertation

1. J.S. Ferreira, A.J.J. Straathof, T.T. Franco and L. A. M. van der Wielen, Activity and stability of immobilized penicillin amidase at low pH values, [J. Mol.Catal. B Enzym., 27 \(2004\) 29-35](#) .
2. J.S. Ferreira, A.J.J. Straathof, X. Li, M. Ottens, T.T. Franco, L. A.M. van der Wielen, Solution crystallization kinetics of 6-aminopenicillanic acid. [Ind. Eng. Chem. Res. 45 \(2006\) 6740 - 6744](#)