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Substrate Inhibition in ω-transaminase Catalyzed Reaction

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For many synthetic processes in the chemical and pharmaceutical industries, highly selective reactions are required. While biocatalysis frequently results in highly selective conversions [1], in many cases, the substrate and the product may inhibit or damage the biocatalyst or interfere with other components in the reaction medium above a critical concentration [2]. One solution is to introduce an auxiliary phase in the form of a solid resin [3]. A solid resin has several advantages over the alternative methods of supply such as organic solvents [4]. This technology uses the resin to act as a 'reservoir' for the substrate and the product. The substrate, via mass transfer, will slowly diffuse into the solution. The slow release will maintain the aqueous concentration beneath an inhibitory level. The biocatalyst will convert the substrate to product which can subsequently be recovered by means of *in-situ* product removal (ISPR). When the resin is saturated, the product is eluted to give a high concentration solution. Such an approach will be investigated in this project. This therefore represents a novel way of intensifying bioprocesses, via the combination of controlled substrate supply, reaction and product removal in an integrated unit operation.

In order to test this hypothesis, a ω-transaminase (ω-TAm) catalyzed reaction for the asymmetric synthesis of (S)-(-)-α- methylbenzylamine (MBA) using isopropylamine (IPA) as amine donor and acetophenone (APH) as amine acceptor was selected. This reaction mechanism was selected since MBA is known to be a very important building block of several pharmaceutical products [5]. However, specific challenges have to be addressed in this system which includes high product and substrate inhibition, unfavourable equilibrium and low substrate solubility [6]. A broad range of polymeric adsorbents comprising various surface areas, pore volumes and functional groups were used in experiments to quantify the partition coefficient and overall capacity of the resin for the substrate and product. It is very critical to select the appropriate adsorbent as the rate of release of the substrate should complement the rate of reaction. The resin can also be loaded with a higher concentration of the substrate. With the selection of the appropriate resin, it was loaded with substrate and released into the reaction media. To make a comparison, the same reaction was carried out by adding the substrate directly to the reaction media. From the experimental findings, it can be stated that the presence of resins had a significant positive impact with respect to biocatalytic activity. The substrate inhibition could be alleviated and allow the reaction to go to completion.

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