

Extractive Fermentation Employing Adsorbent Resin to Enhance Production of Metabolites Subject to Product or Byproduct Inhibition

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Feedback inhibition is a common problem during fermentation process when the concentration of the end product reaches a certain level. The excessive accumulation of byproducts in the culture may also inhibit growth of cell and repress the secretion of the target metabolite. Integration of fermentation and separation of fermentative products or byproducts is the possible approach to be used industrially to reduce product or byproduct inhibition aim at enhancement of fermentation performance. Production of many antibiotics, amino acids and fungal metabolites are subject to feedback inhibition, where the problem shall be reduced to enhance the product yield. On the other hand, production of some metabolites by microorganisms, such as lactic acid bacteria and recombinant bacteria, are subject to byproduct inhibition. In recent years, commercial production of proteins and metabolites from microbial fermentation for industrial applications has increased significantly. Innovative fermentation shall be developed to replace the conventional methods to ensure that the process is economically viable and the price of products become competitive.

To overcome the problem related to feedback repression and the accumulation of the undesirable by-products in the culture, many strategies such as genetic modification, application of fed-batch fermentation, adsorptive membranes, electrodialysis and macroporous ion-exchange resins have been proposed. Inclusion of macroporous adsorbent resin in the culture in combination with effective fermentation may be used as effective approaches to reduce feedback inhibition or to reduce the accumulation of repressive byproducts. This, will in turn, may increase the product yield.

Improvement in antibiotics production in actinomycete fermentation by using the polyaromatic resin Diaion HP-20 has been reported [1]. Inclusion of an adsorbent resin in the production media can also be used to reduce the self-toxicity of the fungal metabolite [2]. Extractive fermentation of *Burkholderia thailandensis* E264 for enhancement of the production of Thailandepsin A, natural product with potent histone deacetylase inhibitory activities and promising anticancer activities, has also been reported [3]. The feedback inhibition of thailandepsin A could be reduced effectively by adding polyaromatic adsorbent resin Diaion HP-20 into the culture, which in turn, significantly increased the titer of the target product. The removal of acetate as it is formed by anion-exchange resin has been successfully used to enhance the recombinant interferon- α 2b production by *E. coli* [4]. With the presence of anion-exchange resins in the culture, physiology of *E. coli* cell was not altered or changed throughout the cultivation. The adsorption capacity of acetic acid by the resins was depended on resins characteristics and matrix. Acetic acid uptake capacity and affinity were higher in weak base anion-exchange resin as compared to strong base anion-exchange resin. This successfully applied in 2 L stirred tank bioreactor with improvement in the production of recombinant interferon- α 2b by about 1.8 times as compared to fermentation without the addition of resins. Since the anion-exchange resins are reusable, the development of bioreactor system with in situ addition of anion-exchange resin for efficient removal of acetic acid may be applied for efficient cultivation of recombinant *E. coli* for production of biotechnology products.

Based on the above information, it seems that the use of adsorbent resin is very promising to overcome the problem in feedback inhibition due to the accumulation of product and byproduct in the culture. Research and development in this fermentation approach shall be extended to various fermentation processes for better understanding. The adsorption capacity of product or byproduct by the resins is depended on resins characteristics and matrix, in which, some information on these shall be generalized. The important factors in scaling-up of the process approach shall be identified. Kinetic models that can be used to describe the process is also required, which could be used as references for developing large-scale extractive fermentation for improvement of metabolite production subject to product or byproduct inhibition. Publication in this area of research and development in Open Access Journal of Fermentation Technology will help scientists and technologists to work together to make repositories of research findings, which can ensure continued access to scholarly publications into the distant future. Publication in open access also helps libraries in undeveloped areas around the world to have greater access to the scholarly resources. In addition, OMICS group also provides user friendly of feasible website-translation of published paper in Fermentation Technology to more than 50 languages, which enable worldwide communication with researchers in the area of interest. Views and opinions from researchers worldwide on the published articles can also be discussed and shared in various social networking such as Face book and Twitter.

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