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Development of a three-zone simulated moving bed process based on partial-discard strategy for continuous separation of valine from isoleucine with high purity, high yield, and high product concentration

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ABSTRACT

The issue of separating valine from isoleucine has been a major concern in the biotechnological process for production of valine. To address this issue, an optimal three-zone simulated moving bed (SMB) process for continuous separation of valine was developed in this study. It was first found that an Amberchrom-CG161C resin was highly suitable for the adsorbent of such SMB process. The adsorption isotherm and mass-transfer parameters of valine and isoleucine on the Amberchrom-CG161C adsorbent were then determined through multiple frontal experiments. The determined parameters were used in the next stage of optimizing the SMB for valine separation, which was performed on the basis of genetic algorithm. For the optimized SMB process, a partial-discard strategy was applied to the raffinate port in order to make a further improvement in the valine product concentration. Finally, the optimized SMB based on the partial-discard strategy was tested experimentally using the self-assembled SMB equipment. The experimental results showed that the developed process in this study was highly effective in continuous separation of valine from isoleucine while ensuring the attainment of high product concentration. The experimental data for the SMB effluent histories and the SMB column profiles were also in close agreement with the model predictions.

1. Introduction

Several branched-chain amino acids have been highly useful in a variety of industries. One of such amino acids is valine, whose noteworthy applications include pharmaceuticals, cosmetics, and animal feed additives [1–4]. Such a wide usefulness of valine has led to an increase in its market demand.

At present, a well-established way of producing valine is to utilize biotechnological processes with bacteria of the species *Corynebacterium* [1–4]. One of the important issues in such processes is that a side-product (isoleucine) is generated along with a target product (valine). To ensure the economic feasibility of the valine production, it is essential to develop a highly efficient large-scale process for separation of valine (target product) from isoleucine (side-product). A key requirement for ensuring high economical efficiency in a separation process is generally to operate it in a continuous mode, i.e. to perform the continuous loading of a feed mixture and the continuous collection of a product [5]. Among such type of processes, it is worth paying particular attention to a simulated moving bed (SMB) chromatographic process, which has proved to be highly suitable for separating bioproducts in a continuous mode [5–8].

The main features of the SMB process are (1) to utilize multiple chromatographic columns and multiple ports and (2) to move the ports periodically in the direction of liquid flow, thereby creating the effect of counter-current contact between solid (adsorbent) and liquid phases [5–8]. If the flow rates and port switching interval are properly determined under such circumstances, a feed mixture can always be made to be loaded into the overlapping region of two solute bands while a product can always be made to be withdrawn from the separated region. Since this operation pattern not only allows a continuous feed-loading and a continuous

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product-collection but also guarantees high purity and high yield, the SMB process can achieve higher economical efficiency than other batch separation processes [8–11].

There are three main considerations for developing such an SMB process for the separation task of interest in this work. First, a reliable adsorbent with large particle size and high selectivity between valine and isoleucine should be employed. Secondly, the SMB process to be developed should be well optimized to guarantee high economical efficiency, high purity, and high yield. Thirdly, the optimized SMB process should be validated through a well-organized process experiment.

The goal of this study is to accomplish the aforementioned tasks. For this purpose, a series of preliminary pulse tests had been performed in advance using several commercial adsorbents with the particle sizes larger than 100 μm. It was found from the results of the preliminary tests that an Amberchrom-CG161C resin could become a highly suitable adsorbent for valine separation. Based on this adsorbent, an optimal three-zone SMB process for continuous separation of valine from isoleucine was developed in this study.

As a first step for this work, the intrinsic parameters of valine and isoleucine on the Amberchrom-CG161C resin were determined through a series of multiple frontal experiments. The determined parameters were then used in the optimization of the three-zone SMB process for valine separation (Fig. 1), which was performed on the basis of non-dominated sorting genetic algorithm with elitism and jumping genes (NSGA-II-JG) [12,13]. In addition, a partial-discard strategy [14–16] was applied to the optimized SMB process in order to make a further improvement in the valine product concentration. This could definitely be a meaning application because the attainment of high valine product concentration is effective in reducing the amount of the stream loaded to subsequent crystallization process, which can contribute to an increase in the throughput of the subsequent process. Finally, the optimized SMB process based on the partial-discard strategy was tested experimentally using a laboratory-scale SMB equipment that was configured to have three zones (Fig. 2). The SMB experimental results showed that the developed process in this study was successful in continuous separation of valine with high throughput, high purity, high yield, and high product concentration.

2. Theory

2.1. Detailed model for simulation of an SMB process

One of the important tasks for a successful development of SMB process is the computer-assisted simulation based on detailed column model, through which the solute migration behaviors in each column of SMB can be predicted with high accuracy. The predicted results from such simulations can provide an opportunity for checking in advance whether the SMB process will function properly and thus attain the targeted separation goal [16]. This can reduce the number of process experiments required, and make it easier to explore a potential strategy for improving the process performance. Furthermore, the simulation model can readily be incorporated into a well-established optimization routine such as genetic algorithm, which is recognized to be highly effective in optimizing SMB processes. Hence, the targeted SMB process in this study will be developed in accordance with a systematic model-based approach.

Until now, several kinds of column models for simulation of a multi-column process have been reported in the literature. Such models include the ideal equilibrium model, equilibrium dispersive model, lumped mass-transfer model, and general rate model [5–7,17]. Among them, the lumped mass-transfer model was chosen as the simulation model of this study because it has sufficient advantages in the aspects of both accuracy and computation time, and its effectiveness in predicting the separation behavior of a multi-column process has been verified in many of previous studies [5–7,11,13,16,17]. This model considers convection, axial dispersion, and mass-transfer between the mobile phase and the solid phase (or adsorbent phase). The corresponding model equations for each column are presented below [5–7,11,13,16,17].

$$\varepsilon_b \frac{\partial C_{b,i}}{\partial t} + (1-\varepsilon_b) K_{f,i}(C_{b,i} - C_i^*) + u_0 \varepsilon_b \frac{\partial C_{b,i}}{\partial z} - \varepsilon_b E_{b,i} \frac{\partial^2 C_{b,i}}{\partial z^2} = 0 \quad (1a)$$

$$\varepsilon_p \frac{\partial C_i^*}{\partial t} + (1-\varepsilon_p) \frac{\partial q_i}{\partial t} = K_{f,i}(C_{b,i} - C_i^*) \quad (1b)$$

where the subscript i stands for different solutes; $C_{b,i}$ is the mobile-phase concentration; C_i^* is the average pore-phase concentration; q_i is the solid-phase concentration, which is in equilibrium with C_i^*; ε_b is the bed voidage; u_0 is the liquid interstitial velocity; ε_p is the particle porosity; and E_b is the axial dispersion coefficient. In addition, K_f is the lumped mass-transfer coefficient, which can be estimated from the following equation [5–7,11,17].

$$\frac{1}{K_f} = \frac{(d_p/2)^2}{15\,\varepsilon_p D_p} + \frac{(d_p/2)}{3\,k_f} \quad (2)$$

where d_p is the diameter of adsorbent particle; D_p is the intra-particle diffusivity; and k_f is the film mass-transfer coefficient.

The equilibrium relationship between q_i and C_i^* in the above model equation is usually expressed by an adsorption isotherm, which is given below in the case of a linear adsorption relationship.

$$q_i = H_i C_i^* \quad (3)$$

where H_i is the Henry constant of component i.

To solve the aforementioned model equations, a biased upwind differencing scheme (BUDS) was employed in conjunction with Gear integration having a step size of 0.05. The number of nodes in each column was set at 60. All of these numerical computations were carried out in Aspen Chromatography simulator.

2.2. Optimization tool for optimal design of an SMB process

Another important task in the development of SMB process is to secure the optimal SMB operating parameters, by which its targeted separation can be performed up to a desired level while maximizing throughput (or productivity). This task has been referred to as SMB design, which has necessitated the preparation of an efficient and accurate tool of SMB optimization.

There are several SMB optimization tools or methods available in the literature. Among them, it is worth mentioning first the standing wave design (SWD) method [5,17], which is computationally efficient while considering mass-transfer effects in the SMB optimization. However, the SWD method does not reflect the periodic port switching in SMB as it is, but follows the principle of true moving bed [5,17], which sometimes causes difficulties in obtaining accurate optimum solutions under realistic conditions, particularly for the SMBs with one column per each zone. It was reported that only the optimization tools based on the considerations of (1) mass-transfer effects and (2) periodic port switching could guarantee high purity and high yield under realistic conditions [9,15–17]. The preparation of such optimization tools usually requires the detailed column model to serve as the basis of SMB optimization. In regard to such SMB optimization based on the detailed column model, the non-traditional optimization methods based on stochastic search techniques are known to be more effective in finding out the optimal solutions, compared to the traditional optimization methods