Modifier mass transfer kinetic effect in the performance of solvent gradient simulated moving bed (SG-SMB) process

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Abstract. The solvent-gradient simulated moving bed process (SG-SMB) is the new tendency in the performance improvement if compared to the traditional isocratic solvent conditions. In such SG-SMB separation process the modulation of the solvent strength leads to significant increase in the purities and productivity followed by reduction in the solvent consumption. A stepwise modelling approach was utilized in the representation of the interconnected chromatographic columns of the system combined with lumped mass transfer models between the solid and liquid phase. The influence of the solvent modifier was considered applying the Abel model which takes into account the effect of modifier volume fraction over the partition coefficient. The modelling and simulations were carried out and compared to the experimental SG-SMB separation of the amino acids phenylalanine and tryptophan. A lumped mass transfer kinetic model was applied for both the modifier (ethanol) as well as the solutes. The simulation results showed that such simple and global mass transfer models are enough to represent all the mass transfer effect between the solid adsorbent and the liquid phase. The separation performance can be improved reducing the interaction or the mass transfer kinetic effect between the solid adsorbent phase and the modifier. The simulations showed great agreement fitting the experimental data of the amino acids concentrations both at the extract as well as at the raffinate.

1. Introduction

The simulated moving bed (SMB) process has been implemented successfully in the pharmaceutical industry to perform difficult separation of molecules. The simulated moving bed (SMB) is a continuous process of interconnected high-performance liquid chromatographic (HPLC) columns which can be used to separate enantiomeric mixtures with high purity and low solvent consumption. The process consists in the simulated countercurrent movement of solid adsorbent phase by switching the positions of the two inlet (Feed and Desorbent) and the two outlet (Extract and Raffinate) streams in the clockwise direction. The more and less adsorbable molecules of enantiomers are collected in the extract and raffinate stream, respectively.

The solvent-gradient simulated moving bed process (SG-SMB) is the new tendency in the performance improvement if compared to the traditional isocratic solvent conditions [1-2]. In such SG-SMB process the modulation of the solvent strength leads to significant increase in the purities and productivity followed by reduction in the solvent. The solvent strength in the SG-SMB process is altered through the volume fraction of the modifier (φ) as can be seen in Fig. 1. Nam et al. [1] carried out SG-SMB experiments in the performance evaluation of phenylalanine and tryptophan separation

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which was compared to isocratic solvent conditions. Its operating conditions were determined from the SG-SMB optimization tool based on genetic algorithm.

![Figure 1 – Schematic representation of SG-SMB](image)

The utilization of modifier (ethanol) to modulate the strength of the solvent in SG-SMB process brings the question about the influence of modifier adsorption on the adsorbent phase over the separation performance. So this work focus on the study of modifier adsorption over the separation performance of SG-SMB applying a linear mass transfer kinetic model for the modifier combined with stepwise modelling approach for the chromatographic column representation.

### 1. Modelling and optimization approaches

The chromatographic columns of the SG-SMB process are modeled as a discrete representation of N mixed cells in series combined with lumped mass transfer solid-liquid model,

$$\frac{dC_i^\text{p}}{dt} + \frac{dq_i^\text{p}}{dt} = (C_i^\text{p} - C_i^0)\sigma_i^\text{p}$$  \hspace{1cm} (1)

in which $C_i^\text{p}$, $C_i^0$, $q_i^\text{p}$ and $t$ represents the concentration of compound $i$ in the liquid phase, the concentration of compound $i$ in the liquid phase at the entrance of the mixed cell, the concentration of compound $i$ in the solid adsorbent phase and the time, respectively, all at column $p$. In Eq. 1 $\sigma_i^\text{p} = F/\epsilon V$ with $F$, $\epsilon$ and $V$ representing the volumetric flow rate, the total porosity and the volume of the mixed cell, respectively. It was utilized the Abel’s model for the determination of the partition coefficient ($K$)

$$K = \frac{p_1}{(1+p_2 \phi)^p_3}$$  \hspace{1cm} (2)

where $p_1$, $p_2$ and $p_3$ are the model parameters of either tryptophan or phenylalanine.

The following linear mass transfer kinetic model is applied both for the solutes as well as for the modifier (ethanol)

$$\frac{dq_i^\text{p}}{dt} = \tau_i C_i^\text{p} - \sigma_i q_i^\text{p}$$  \hspace{1cm} (3)

in which $\tau_i$ and $\sigma_i$ correspond to the mass transfer kinetic parameter in the adsorption and desorption, respectively. The residence times of the two kinds of molecules (phenylalanine and tryptophan) were utilized in the columns characterization for the determination of the mass transfer parameters of the lumped mass transfer model (Eq. 3). For each aminoacid in each condition of the volume fraction of modifier ($\phi = 0$, 0.05 and 0.2) it was determined the mass transfer parameters of adsorption and desorption that led to the same experimental value of residence time [3]. For the modifier the mass transfer parameters were get through the Lagmuir isotherm equation obtained in the literature [4]

### 3. Results and discussions

The Fig. 2 shows the effect of mass transfer adsorption parameter of modifier (ethanol), $\tau_i$, over the separation performance of the aminoacids phenylalanine and tryptophan. The results of Fig. 2 are in terms of concentration along the chromatographic columns. It can be noted from Fig. 2A to 2C that the mass transfer adsorption parameter of modifier, $\tau_i$, was increased keeping the equilibrium constant ($K_{eq}$) leading to an increase in the adsorption of modifier on the solid adsorbent phase. Such procedure altered the concentration of modifier in the liquid phase which becomes more distributed along the columns as it can be seen in Fig. 2C (vide dotted line). The distribution of modifier along the columns
altered the concentration profiles of the aminoacids along the columns which become wider reducing the purity in the extract as well as raffinate (see Table 1).

![Figure 2 – Amioacids concentration along time according to different values of mass transfer kinetic of modifier; \( \phi_0 = 0.2 \)](image)

The Table 1 presents the values of purity and productivity according to the mass transfer adsorption parameter values of modifier. As can be seen in Table 1 the reduction in the extract purity is more significant than in the raffinate both contribution to the reduction in the productivity of the SG-SMB process.

| Figure (Fig. 2A) | (Fig. 2B) | (Fig. 2C) |
|------------------|-----------|-----------|
| Adsorption Parameter, \( \tau_i \) [1/s] | 0.0015 | 0.15 | 1.5 |
| Raffinate purity (%) | 99.99 | 99.98 | 97.69 |
| Extract purity (%) | 99.36 | 95.74 | 96.20 |
| Productivity [g/h.L] | 0.581 | 0.548 | 0.508 |

![Table 1 – Separation performance of SG-SMB according to \( \tau_i \)](table)

The Fig. 3 presents the concentration profiles of the phenylalanine and tryptophan along time in the raffinate and extract, respectively. The dotted lines correspond to the cyclic simulations obtained as the streams change the positions along time in the process. The full continuous lines are the average simulations in which the black results correspond to the conditions obtained assuming mass transfer of modifier (ethanol) between the liquid and solid adsorbent phase. The points corresponds to the experimental data obtained by Nam et al. [1]. As can be seen in Fig. 3 there is a better agreement between the simulation results and the experiments for the cases considering the modifier mass transfer effect. The "roll-up" phenomenon (described by Nam et al.[1]) or the peak in the phenylalanine concentration in Fig. 3A was observed in the simulation results which is more evident in the cyclic simulations (dotted lines) of Fig. 3A.

![Figure 3 – Correlation between the simulation (lines) and the experimental data (points)](image)
The Fig. 4 presents the concentration of phenylalanine along the columns showing in detail the concentration in the extract along time. The "roll-up" phenomenon can be also observed in the extract as described in detail in Fig. 4A and 4B. In the transient period of the SG-SMB process there is an increase in the concentration of modifier along time (dotted lines) which reduces the adsorption affinity of phenylalanine releasing such aminoacid from the adsorbent phase to the liquid phase. Therefore there is an increase in the phenylalanine concentration (black line) followed by a decrease (thick gray line) as the molecules migrate forward through the liquid phase. The arrows in Fig. 4 indicate the position the extract stream is collected in the process. In Fig. 4A it was utilized an hypothetical value of mass transfer kinetic only to show clearly the "roll-up" phenomenon. The experimental data of Nam et al. [1] shows the "roll-up" in the extract in detail in Fig. 4B. The values of modifier mass transfer kinetic in Fig. 4B are the same utilized in Fig. 3. It should be noted that the "roll-up" phenomenon in the extract is very small due to the low concentration of phenylalanine in such stream.

![Figure 4 – The "roll-up" phenomenon in the extract](image)

3. Conclusions
The proposed modeling approach based on modifier mass transfer kinetic was able to represent the main phenomenon aspects of the separation of the aminoacids phenylalanine and tryptophan in SG-SMB processes. The modifier mass transfer effect is related to the experimental observation of "roll-up" phenomenon of phenylalanine both in the extract as well as in the raffinate. The separation performance of the SG-SMB process can be improved reducing the interaction or the mass transfer kinetic effect between the solid adsorbent phase and the modifier.

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