SEPARATION STUDY OF BACLOFEN PRECURSOR IN A SMB (SIMULATED MOVING BED) UNIT APLLYING A KINETIC APROACH

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Abstract. The separation of baclofen precursor was analyzed through a SMB (Simulated Moving Bed) experimental unit being the results compared to an equivalent SMB unit with eight chromatografic columns. The experimental results were studied in terms of the transient in the concentrations of raffinate and extract. The variation of concentrations with the columns in the zones was also compared to the simulation results. The SMB was modeled through the kinetic approach assuming competition between the solute molecules. From the simulation results were possible to represent the qualitative aspects of the SMB process achieving the same behavior in the profiles for the concentration of solutes in the extract and raffinate. The concentration of desorbent showed to be very important in the separation process as well the kinetic parameters. The number of cycles of the experimental unit to reach the steady state were obtained with the simulations assuming predetermined kinetic conditions.

Keywords: Simulated Moving Bed (SMB), Kinetic Conditions, Desorbent, Extract, Raffinate

1. INTRODUCTION

The chromatographic separation techniques, such as the simulated moving bed (SMB) processes, which are related to adsorption phenomena, correspond to a very important field for the separation of molecules utilized mainly by the chemical and pharmaceutical industry. The application of the modeling and simulation to study the SMB processes is a key factor for the comprehension and therefore the improvement of such systems.

The modeling of SMB systems can be done applying different mathematical approaches, with respective advantages and limitations according to the method assumed. The application of mass balance models for characterizing the transport phenomena inside the column is a constant in this area. In the modeling of SMB processes the degree of complexity may vary significantly according to the description of the unit operation (plug flow, mixture etc.), the mass transfer resistance (equilibrium, mass transfer resistance etc.) and the adsorption equilibrium (linear, Langmuir etc.) (Rodriguez and Minceva, 2005).

From the publications related to the modeling and simulation of SMB processes can be observed different research groups with different strategies of modeling. The "equilibrium theory" is an example of approach utilized to study different operation conditions of SMB processes (Mazzotti *et al*., 1997, Gentilini *et al*., 1998, Migliorini *et al*., 2000 and Abel *et al*. 2002, 2004). It is interesting in the studies of optimum operation conditions of SMB systems as it simplifies the complex behavior related, generally, to non-linear competitive adsorption phenomenology (Migliorini *et al*., 2000). The "equilibrium theory" assumes immediate equilibrium between the stationary and liquid phase, without considering the effects of axial dispersion and mass transfer resistance. The "equilibrium dispersive" models represent another path followed in the modeling of SMB processes, being observed the incorporation of linear driving force (LDF) methods to represent the adsorption of solute into the adsorbent phase (Zhong and Guiochon, 1997, 1997a, Mihlbachler *et al*., 2001 and Pais *et al*. 1998, 1998a). In such models are considered both the axial dispersion and the convection along the column. An application of the "equilibrium dispersive" theory can be observed through the study of the effects of the columns porosity in the performance of SMB processes with and without linear adsorption conditions (Mihlbachler *et al*., 2001). From that it was observed that the rate of production and the solute purity were affected by the fluctuations of the columns characteristics. A comparison between the separation processes by SMB and TMB (true moving bed) (Pais *et al*., 1998) showed that to represent a TMB separation process by a SMB it is necessary to subdivide the SMB columns in a infinite number of parts with switch time close to zero. However, the results obtained with SMB and TMB were equivalent, presenting small deviation, which validate the application of SMB models in the studies of TMB processes.

The utilization of equilibrium isotherms to represent the adsorption behavior of the chromatographic columns of SMB processes is widely observed, because the use of continuous chromatographic processes has been pointed to as an important tool to meet the objectives of the chemical manufacture of several chiral compounds (Nicoud, 1999). The SMB is a large-scale version of tradicional high-performance liquid chromatography (HPLC), but unlike normal HPLC, it operates continuously, without loss of the enantiomeric purity of the outlet streams. The process consists in simulating the countercurrent movement of the bed of adsorbent by switching the positions of the inlet and outlet streams, producing two outlet streams, one rich in the more adsorbable component (extract steam) and the other rich in the less adsorbable one (raffinate stream), which is adequate for binary separations, as in the case of racemates. SMB has been used by several authors to separate components from racemic mixtures (Juza et al., 2000), obtaining the two enantiomers of a chiral molecule with a high enough purity and in sufficient quantities to carry out clinical tests or even production stages.

. As the SMB systems works through "pseudo-stationary" regimes, which depends on the switch time for each configuration, the adoption of models that represent the dynamic behavior of the adsorption is an important step to comprehend the separation mechanisms. In this work a SMB process formed by 8 interconnected chromatographic columns was modeled through mixture mass balance models with kinetic mechanisms of competitive adsorption. The applied modeling permitted to study the transient behavior of the SMB system through the analysis of the kinetic parameters over separation mechanisms. The simulation results were compared to experimental data obtained by (Veredas *et al*., 2006).

2. PROCESS MODELING

The SMB process was represented by 8 interconnected chromatographic columns (I, II, III, IV, V, VI, VII and VIII) as shown in Fig. 1., in which F, D, R and E correspond to the flow of feed, desorbent (solvent), raffinate and extract, respectively.

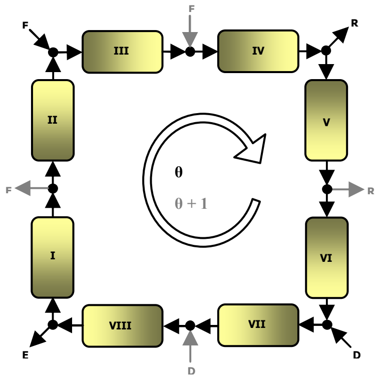

Figure 1. Representation of the SMB process

The liquid flow and the configurations of the cycle F-R-D-E-F follow the clockwise according to the switch time, which is the time spent in each configuration. As the liquid phase follows in the clockwise direction the adsorbent solid phase follows in the anti-clockwise by "Simulated" movement (SMB-*Simulated Moving Bed*).

The solutes A and B were represented as the more and less retained molecules, being determined by the following kinetic mechanisms of adsorption (Fig. 2). The mechanisms below correspond to competitive adsorption, i.e. the solutes A and B can be adsorbed by the same adsorption sites of adsorbent solid phase (s).

$$\begin{array}{cc} \mathrm{A} + s \xrightarrow{k_1} \mathrm{A}.s & \mathrm{A}.s + D \xrightarrow{k_3} \mathrm{A} + D + s \\ \mathrm{B} + s \xrightarrow{k_2} \mathrm{B}.s & B.s + D \xrightarrow{k_4} \mathrm{B} + D + s \\ \text{(a)} & \text{(b)} \end{array}$$

Figure 2. Kinetic mechanisms of adsorption of solutes A and B (a) with respective desorption (b)

The adsorption of solutes A and B are represented by the kinetic constants of adsorption, k_1 and k_2, respectively, which depends on the solute concentration (A or B) and the concentration of adsorption sites (s). The desorption, through the kinetic constants of desorption, k_3 and k_4, for the solutes A and B, respectively, depends on the concentration of solvent (D) and the concentration of solute adsorbed on the solid phase.

According to the kinetic mechanisms shown in Fig. 2 it can be written the consumption rate of solutes A and B by the adsorbent solid phase. The consumption rate of solute A, $(-r_A)$, is given by

$$(-r_A) = k_1.C_A.C_S - k_3.q_A.C_D \qquad (1)$$

where C_A, C_S, q_A and C_D represent the concentration of solute in the liquid phase, the concentration of adsorption sites on the adsorbent, the concentration of solute A adsorbed in the solid phase and the concentration of desorbent, respectively. Applying the mass balance models of perfect mixture (Câmara and Silva Neto, 2006) combined with the consumption rate models of Eq. 1 we determined the following equations, exemplified for the solute A.

$$\frac{dC_{A,p}}{dt} = \left[\ c_1.C_{A0} - c_1.C_A - (k_1.C_A.(q_m - q_A - q_B) - k_3.q_A.C_D)\ \right]_p \tag{2}$$

$$\frac{dq_{A,p}}{dt} = \left[\ k_1.C_A.(q_m - q_A - q_B) - k_3.q_A.C_D\ \right]_p \tag{3}$$

$$\frac{dC_{D,p}}{dt} = \left[\ c_1.C_{D0} - c_1.C_D\ \right]_p \tag{4}$$

with the parameter $c_1 = Q / \varepsilon .V$, in which q_m, ε, V and Q correspond to the maximum adsorption capacity, the column bed porosity, the column volume and the volumetric flow, respectively. The first term of Eq. 2 corresponds to the accumulation, being the second, third and fourth the terms of solute entering, the solute exiting and the consumption rate, respectively, for each column p. More details about the application of kinetic mechanisms to study chromatographic processes can be found in Câmara and Silva Neto (2006).

Through the configuration of the SMB process shown in Fig. 1 it was obtained the global mass balance

$$Q^F + Q^D = Q^R + Q^E \tag{5}$$

$$Q^I = Q^{CTE} \tag{6}$$

$$Q^{II} = Q^I \tag{7}$$

$$Q^{III} = Q^{II} - Q^E \tag{8}$$

$$Q^{IV} = Q^{III} \tag{9}$$

$$Q^V = Q^{IV} + Q^F \tag{10}$$

$$Q^{VI} = Q^V \tag{11}$$

$$Q^{VII} = Q^{VI} - Q^R \tag{12}$$

$$Q^{VIIII} = Q^{VII} \tag{13}$$

The roman numbers (I, II, III, IV, V, VI, VII and VIII) correspond to each column in Fig. 1. The mass balance eqs. (6-13) must be recalculated after each clockwise change of positions F, R, D and E, having a complete cycle after the 8th change, in which the initial configuration is repeated.

3. RESULTS AND DISCUSSION

The simulation results presented in this article were obtained utilizing the parameters listed in Table 1 for most of the cases studied. The parameters of Table 1 are related to the experimental conditions of the work of Veredas *et al.*, 2006. As can be seen from Table 1, the molecule A is the more retained substance by the adsorbent phase as it has the higher kinetic constant of adsorption.The system of ordinary differential equations for the mass balance models of compounds A, B and D were solved numerically utilizing the Runge Kutta's method of 4th order.

Table 1- Parameters utilized in the simulations

Maximum capacity (mg/mL)	$q_m^{I,II}$	$q_m^{III,IV}$	$q_m^{V,VI}$	$q_m^{VII,VIII}$
	50	50	50	50
Kinetic constants (mg/mL.min)	k_1	k_2	k_3	k_4
	20	0.5	4	0.4
Conc. (mg/mL)	C_A^F	C_B^F	C_D^F	C_D^D
	1.5	1.5	0	40
Vol. flow (mL/min)	Q_F	Q_R	Q_D	Q_E
	0.1	0.39	0.73	0.44
Others	e (porosity)	V(mL)	ST(min)	h (numeric step)
	0.66	7.5	25	0.001

Figure 3 presents the comparison between the simulation results (lines) and the experimental data from Veredas *et al.*, 2006, in terms of concentrations of solutes A and B at the extract. The experimental condition corresponds to the SMB separation of 7 cycles of 200 min each.

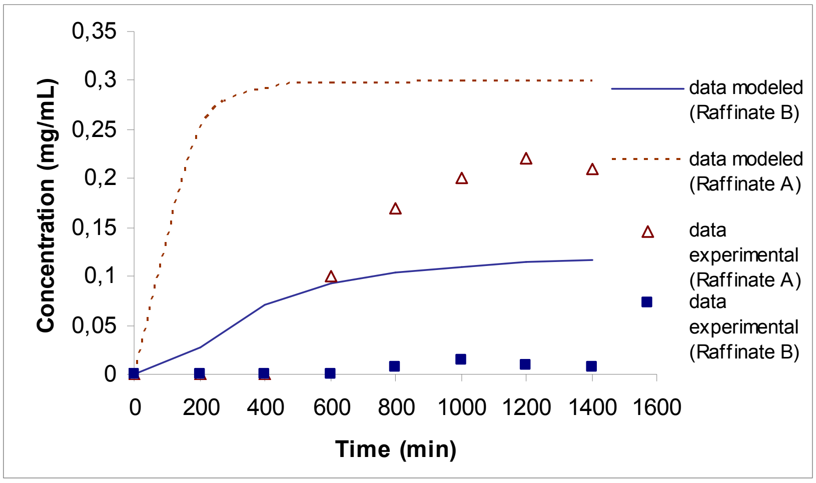

Figure 3. Concentration profile for the stream

As can be seen from Fig. 3 the concentration of solute A is higher at the extract if compared to solute B. The dynamical profiles of the experiments were not well fit by the simulations although the calculations represented the steady states conditions after 1200 min or 6 cycles. The time to achieve the steady state was observed from the simulations in which for solute B was around 400 min and 1200 min for solute A. Therefore the solute B achieves the steady state earlier than solute A. Can be noted that the experimental profiles are similar to the simulations profiles if we could eliminated the initial time without concentration (after 400 min).

Figure 4 shows that the simulation results (according to each section of the SMB unit) of separation of solutes A and B at the extract and raffinate after 7 cycles or 1200 min. The profiles show that in the first stage of separation the concentration of solute A at extract was higher than that of solute B, while the concentration at raffinate was the inverse, i.e. higher concentration of solute B.

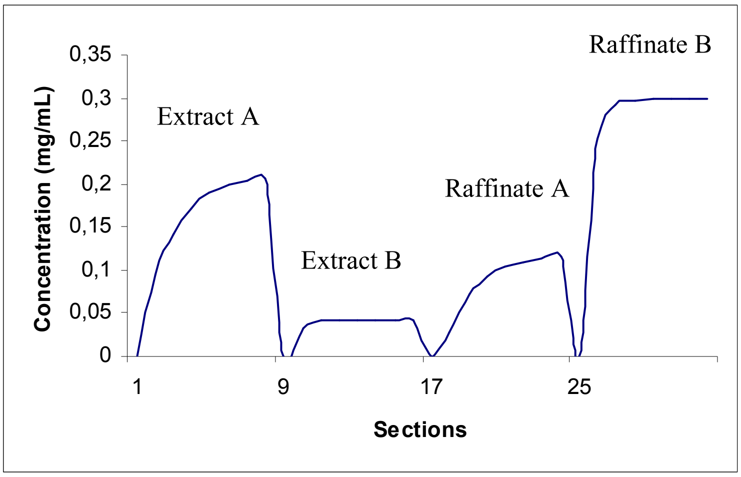

Figure 4. Concentrations profiles of solutes A and B at the extract and raffinate

Fig. 5 presents the experimental (Veredas *et al*., 2006) and calculated concentrations along the 8 columns of the SMB unit. Can be observed that the solute A is more concentrated from column 1 to 4 while the solute B is more concentrated from column 4 to 8. From Fig. 5 can be seen that the simulations represented the separation sections of solute A and B although the fit with the experiments was not satisfactory.

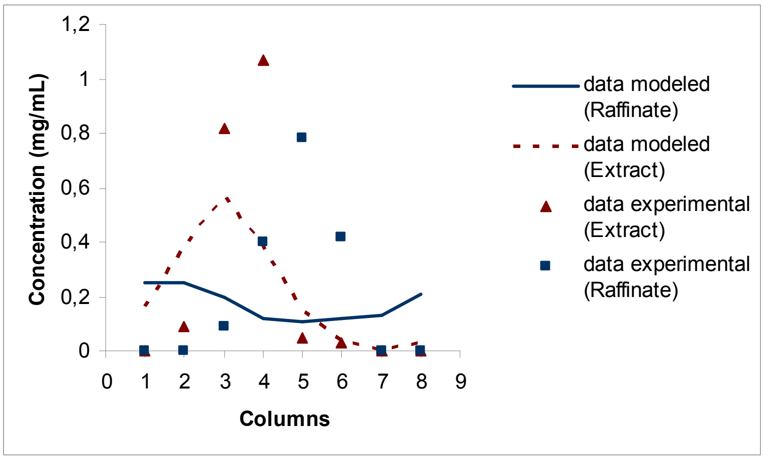

Figure 5. Internal profile for the SMB system in the steady state

Another important observation from Fig. 5 is that the simulations results can be used to indicate the best position in the SMB unit to locate the extract and raffinate streams. From it a good point for withdrawing the raffinate stream is located between columns 6 and 7, while that for the extract is located between columns 2 and 3, with the feed stream being introduced near the columns 4 and 5.

4. CONCLUSIONS

From the present work of modeling of a SMB separation process by mass mixture models through adsorption kinetic phenomenology was possible to simulate the main aspects of SMB systems related to transient and "pseudo-stationary" regime. From the simulations results were observed a great dependence of the kinetic parameters and the maximum capacity of adsorption over the purity of the products obtained at the raffinate and extract. The switch time (ST) showed to be decisive to achieve the optimum conditions of separation.

The concentration obtained by the extract indicates a higher adsorption capacity and hence greater ease in entering the steady state in relation to raffinate.

The solute B has a lower adsorption compared with the solute A, taking longer and a greater number of cycles to enter the steady state.

Note that in modeling the separation of the substances showed a significant result to obtain qualitative data on the experimental study. The case study shows that in seven complete cycles of 200 minutes each there is greater tendency toward steady state.

5. ACKNOWLEDGEMENTS

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