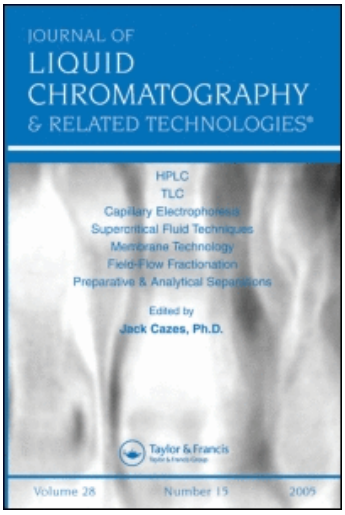

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Design and Sensitivity Analysis of Simulated Moving Bed Chromatography to Separate Sugar Alcohols

Ju Weon Lee[a]; Jin-Il Kim[b]; Chong Ho Lee[c]; Jeung Kun Kim[c]; Yoon-Mo Koo[b]
[a] Department of Chemical Engineering, Inha University, Nam-ku, Inchon, Republic of Korea [b] Department of Biological Engineering, Inha University, Nam-ku, Inchon, Republic of Korea [c] Center for Advanced Bioseparation Technology, Inha University, Inchon, Republic of Korea

To cite this Article Lee, Ju Weon , Kim, Jin-Il , Lee, Chong Ho , Kim, Jeung Kun and Koo, Yoon-Mo(2007) 'Design and Sensitivity Analysis of Simulated Moving Bed Chromatography to Separate Sugar Alcohols', Journal of Liquid Chromatography & Related Technologies, 30: 13, 1859 — 1877
To link to this Article: DOI: 10.1080/10826070701386413
URL: http://dx.doi.org/10.1080/10826070701386413

Journal of Liquid Chromatography & Related Technologies®, 30: 1859–1877, 2007

ISSN 1082-6076 print/1520-572X online
DOI: 10.1080/10826070701386413

Design and Sensitivity Analysis of Simulated Moving Bed Chromatography to Separate Sugar Alcohols

Ju Weon Lee
Department of Chemical Engineering, Inha University, Nam-ku, Inchon, Republic of Korea

Jin-Il Kim
Department of Biological Engineering, Inha University, Nam-ku, Inchon, Republic of Korea

Chong Ho Lee and Jeung Kun Kim
Center for Advanced Bioseparation Technology, Inha University, Inchon, Republic of Korea

Yoon-Mo Koo
Department of Biological Engineering, Inha University, Nam-ku, Inchon, Republic of Korea

Abstract: As the advanced unit operation of batch chromatography, the simulated moving bed (SMB) chromatography is widely used in sugar industries with the ion exchange resin as the stationary phase. The conventional SMB process is composed of 4 zones which have different roles. We considered the SMB process to separate two sugar alcohols, xylitol, and maltitol, which are commercially used as alternative sweeteners. To decide the optimum operating condition of the SMB process, we consider the migration velocities of solutes in each zone. The migration velocity of a solute is dependent on the adsorption isotherm and velocity ratio of the mobile phase and the simulated stationary phase velocities. The total concentration of a sugar alcohol mixture in a feed stream and length of the column (10 cm, 15 cm, 20 cm, and 30 cm) were changed to find the optimum column length and operation

Address correspondence to Yoon-Mo Koo, Department of Biological Engineering, Inha University, 253 Yonghyun-dong, Nam-ku, Inchon 402-751, Republic of Korea. E-mail: ymkoo@inha.ac.kr

sensitivities of the feed condition. The adsorption behaviors of two sugar alcohols were the linear isotherms. The isotherm parameters were determined by the single step frontal analysis. The robust operating condition and optimum column length were decided by considering the sensitivities of purity and yield of products.

Keywords: Simulated moving bed chromatography, Xylitol, Maltitol, Design, Sensitivity analysis

INTRODUCTION

Xylitol is a five carbon sugar alcohol that has been recognized as being a "functional food" because of its significant medical and nutritional applications, among which are limitation of its dental caries and its use as a sweetener for diabetics. Xylitol can also be used to prevent some pathologies, such as insufficiency of glucose-6-phosphate dehydrogenase, acute otitis, experimental osteoporosis, and cystic fibrosis. Xylitol is widely distributed in nature, but it is present in plants and fruits only at low concentrations, making its extraction from natural sources economically unfeasible. Presently, xylitol is produced by catalytic hydrogenation of D-xylose contained in acid hydrolyzates from xylan-rich lignocellulosic raw materials. However, the conversion yield of this process is quite low and the product recovery requires various expensive operations for separation.[1,2]

The SMB process is a kind of continuous unit operation for the chromatographic separation, based on the batch chromatography. There are commonly the following four zones to separate two solutes; well retained solute is desorbed for reuse of adsorbent in zone I, well retained and less retained solutes are separated with the different migration velocities that depends on the flow rate ratio of liquid phase and simulated solid phase in zone II and III, and the less retained solute is removed from the liquid phase by the adsorption to solid phase in zone IV to recycle the liquid phase to zone I. All zones have the same solid phase velocity which is simulated by the ports switching between columns at same time, however, each zone has different liquid phase velocity which is formed by the recycle flow between zone I and IV, two inflows in the feed and desorbent ports, and two outflows in the raffinate and extract ports.[3]

The design of the SMB operating condition is mainly calculated by two methods, called the Triangle theory[4] and the Standing Wave method.[5] These two methods, based on the ideal first order partial differential equation of material balance, excluded the dispersion effect in the bulk liquid phase and the mass transfer between liquid and solid phase. Therefore, this mass balance equation cannot present the demanded zone length. If zone lengths are too short, the D/F factor (the flow rate ratio of the desorbent and the feed stream) must have a large value to perfectly separate solutes. A short interval switching time, high consumption of

desorbent, and production of diluted products in the raffinate and the extract stream occurs. To overcome these problems, the second order PDE (partial differential equation) material balance has to be used to determine the operating condition of the SMB process. When the SMB process is used to separate the products produced by some reactions in the up stream process, and these products are produced under sensitive conditions, it is difficult to constantly maintain the total and individual concentration of products. In our previous work, we also considered the variation of the flow rate of the feed stream.[5] However, the flow rate is easier to control than the concentration or composition of products in the up-stream process.

To design the SMB process to separate sugar alcohols, we considered the ion exchange resin as the separation resin, and two common sugar alcohols, xylitol and maltitol is used as solutes. Xylitol and maltitol are alternative sweeteners and has fewer calories than sugar.[6,7] Xylitol is a five carbon polyol and maltitol is the sugar alcohol derived from maltose. Therefore, it is easy to separate xylitol and maltitol by size-exclusion. To decide the isotherm parameters and kinetic parameters, several frontal analyses were preformed with different concentrations of sugar alcohols in the batch chromatography and the simulation of batch chromatography was carried out. With these isotherm parameters and kinetic parameters, the simulation of the SMB process is carried out with different concentrations and composition of solutes in the feed stream and different lengths of the column.

In this work, we observed the influence of the feed conditions and the column length on the purity and the yield of products. The concentrations of xylitol and maltitol are changed from 0.717 g/dl to 4.304 g/dl and from 2.309 g/dl to 13.852 g/dl, respectively. The column length is changed with 10 cm, 15 cm, 20 cm, and 30 cm.

THEORY

Adsorption Isotherm

The adsorption mechanism of carbohydrates on ion exchange resin is the combination of three exclusions called size, ion, and ligand exclusion. In these exclusion mechanisms, the retention times of carbohydrates are not changed according to the changing of the feed concentration. In this manner, adsorption isotherms of xylitol and maltitol followed the linear isotherm. It is the simplest isotherm type. Equation (1) is the formula of the linear isotherm called Henry's law. In this isotherm, there is no competitive adsorption.

$$q_i = H_i c_i \tag{1}$$

where, H_i is the Henry's constant of I component, q_i and c_i are the concentration of I solute in the stationary phase and the mobile phase, respectively.

Triangle Theory

The triangle theory is based on the design of the true moving bed (TMB) process. In the TMB material balance equation, the migration velocity of solutes can be calculated and this velocity depends on the flow rate ratio of liquid and solid phase. The triangle theory is used to decide the operating condition of the SMB process with following inequalities that describe the separation region of each zone.[2]

$$m_i = \frac{Q_i - \varepsilon_p Q_s}{(1-\varepsilon_p)Q_s} \tag{2}$$

$$H_A < m_1 \tag{3-1}$$

$$H_B < m_2 < m_3 < H_A \tag{3-2}$$

$$-\frac{\varepsilon_p}{(1-\varepsilon_p)} < m_4 < H_B \tag{3-3}$$

where, m_i is the flow rate ratio of zone I, ε_p is the intra-particle void fraction, Q_i and Q_s are the volumetric flow rates of the liquid phase in zone I and the solid phase and, H_A and H_B are the Henry's constant of well retained solute A and less retained solute B, respectively. The m_1 and m_4 are easily controlled by changing the flow rates of desorbent, raffinate, and extract streams. The m_2 and m_3 are related to the switching times of ports and the flow rates of recycle and feed streams. In the $m_2 - m_3$ plane, we can draw a triangular region called the separation region.

Simulation

All simulations are done on a personal computer (Pentium 4™). The equilibrium dispersion model is used to predict the column internal profiles and the history profiles of the extract and raffinate stream:

$$\frac{\partial c_i}{\partial t} + F\frac{\partial q_i}{\partial t} + u\frac{\partial c_i}{\partial x} = D_i\frac{\partial^2 c_i}{\partial x^2} \tag{4}$$

where, F is the phase ratio, $= (1-\varepsilon)/\varepsilon$, u is the interstitial flow rate of mobile phase, and D_i is the axial dispersion coefficient of i solute. To solve this PDE system, the finite difference method (FDM) is used. In batch simulation and SMB simulation, the system dead volume is neglected.[1]

EXPERIMENTAL

Analytical Condition

The quantitative analytical method for sugar alcohols is necessary to analyze the composition of sugar alcohols in a solution, as well as effluent of a column

outlet. In this work, the HPLC system with the Polyamine II column (YMC-Pack) was used. HPLC grade acetonitrile, ethanol, and water (deionized) are used as a mobile phase. The optimum mobile phase condition for 2 sugar alcohols (xylitol and maltitol) is ethanol/acetonitrile/water = 20/65/15 (v/v/v). The flow rate is 1.0 mL/min and this experiment is carried out under room temperature.

Batch Chromatography

Dowex 1X4 anion exchange resin (Sigma-Aldrich Co., USA, MO, 200-400 mesh) is used to separate the binary sugar alcohol mixture (xylitol and maltitol). Xylitol and maltitol are purchased from Sigma-Aldrich Co. (USA, MO). The separation resin is packed into the jacketed glass column (10×300 mm). Deionized water produced by Milli-Q water purification system (Millipore, USA) is used as the mobile phase, and the flow rate of the mobile phase is fixed at 1.0 mL/min. The temperature of the column is maintained on 50°C. The feed concentration of xylitol is changed from 0.717 g/dl to 4.304 g/dl and maltitol is changed from 2.309 g/dl to 13.852 g/dl. The off-line elution profiles are observed by the quantitative analysis of fractionated effluent. The fraction amount of effluent is fixed to 1.0 mL. The frontal analysis method is used to estimate the adsorption isotherm parameters.

RESULTS AND DISCUSSIONS

Estimation of Isotherm Parameters and Dispersion Coefficients

To estimate the isotherm parameters and dispersion coefficients, the various feed concentrations of batch chromatography is needed. The 6 points of feed concentration experiments are carried out. Table 1 describes the feed conditions of batch chromatography for estimation of isotherm parameters and axial dispersion coefficients. Figure 1 shows the comparison of experimental isotherm data and the calculated isotherm curves. In this case, xylitol and maltitol are linear isotherms. The partition coefficients (Henry's constant) of xylitol and maltitol are 0.527 and 0.299, respectively, and the axial dispersion

Table 1. The feed conditions of batch chromatography

	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
Xylitol (g/dl)	0.717	1.435	2.151	2.870	3.587	4.304
Maltitol (g/dl)	2.309	4.617	6.927	9.378	11.540	13.852
Feed volume (mL)	10.0	11.5	10	10	20	10

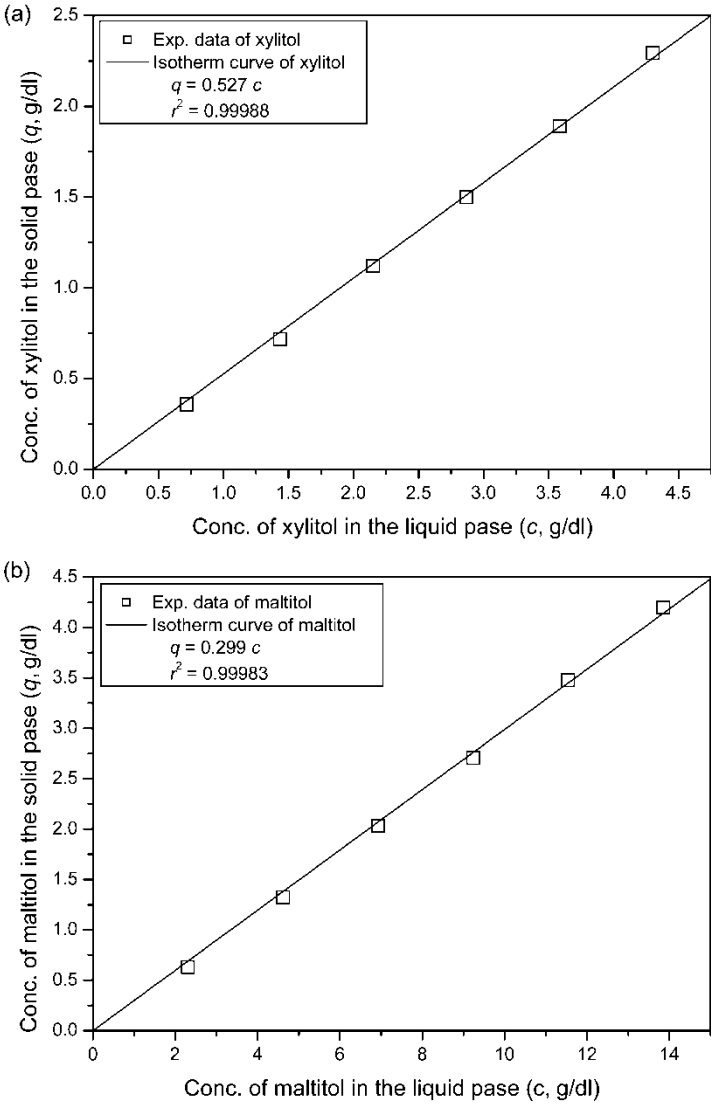

Figure 1. The comparison of experimental isotherm data and calculated isotherm curve of (a) xylitol and (b) maltitol. Open square is the experimental data and solid black line is calculated isotherm curves. r^2 is the regression coefficient.

coefficients are calculated with elution profiles of 6 Runs. Figure 2 shows the changed axial dispersion coefficients of xylitol and maltitol with various inlet concentrations. The axial dispersion coefficients of xylitol and maltitol are similar up to 3.587 g/dl of xylitol and 11.54 g/dl of maltitol. But, the axial dispersion coefficients are very steeply increased when the concentrations of

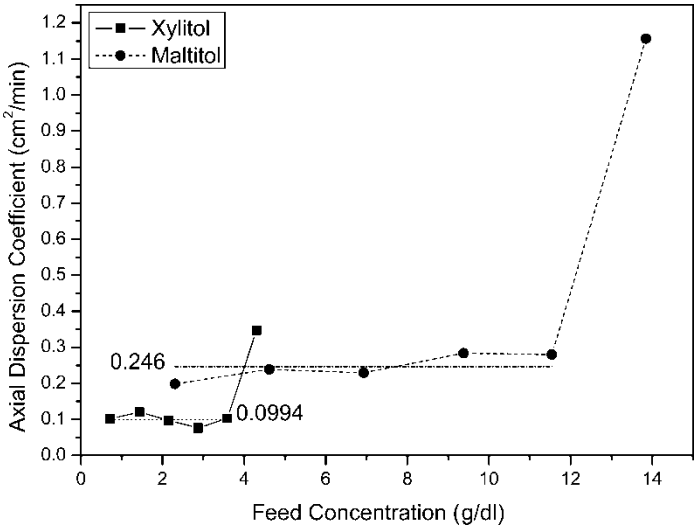

Figure 2. The change of axial dispersion coefficients with various feed concentrations. Black square and line is xylitol and black circle and dashed line is maltitol. The average axial dispersion coefficient values of xylitol and maltitol with 5 points from smallest feed concentration are 0.0994 and 0.246, respectively.

xylitol and maltitol are over 3.587 g/dl and 11.54 g/dl, respectively. Table 2 shows the axial dispersion coefficients of xylitol and maltitol in various ranges of concentration. In SMB simulation, according to the feed concentration of xylitol and maltitol, different axial dispersion coefficients are used. Figure 3 shows the comparison of experimental and simulated elution profiles of 6 Runs (Table 5). In Run 1∼Run 5, axial dispersion coefficients of xylitol and maltitol are fixed as 0.0994 and 0.246 and in Run 6 these values are changed to 0.347 and 1.156, respectively. Run 1∼Run 5 comparisons are in good agreement. Run 6 comparison, however, has some differences in the front of the elution band, but the simulated profile is in good agreement with the experimental data of tailing. Therefore, we used these large values of axial dispersion coefficients for the Run 6 feed condition.

Table 2. The axial dispersion coefficients of xylitol and maltitol

	Xylitol		Maltitol	
Concentration range (g/dl)	0∼3.587	4.304	0∼11.54	13.852
D (cm^2/min)	0.0994	0.347	0.246	1.156

D: Axial dispersion coefficient.

SMB Operating Condition

The triangle theory is used to determine the operating condition of the SMB process. Figure 4 shows the m_2-m_3 plane. The triangle region describes the separation zone and the vertex point is the optimum operating condition for the SMB operation in terms of minimum consumption of desorbent and maximum productivity and enrichment. If the operating point is near the boundary of the separation zone, it is tough to operate SMB practically. Therefore, 4 points of operating conditions including vertex point (Figure 4)

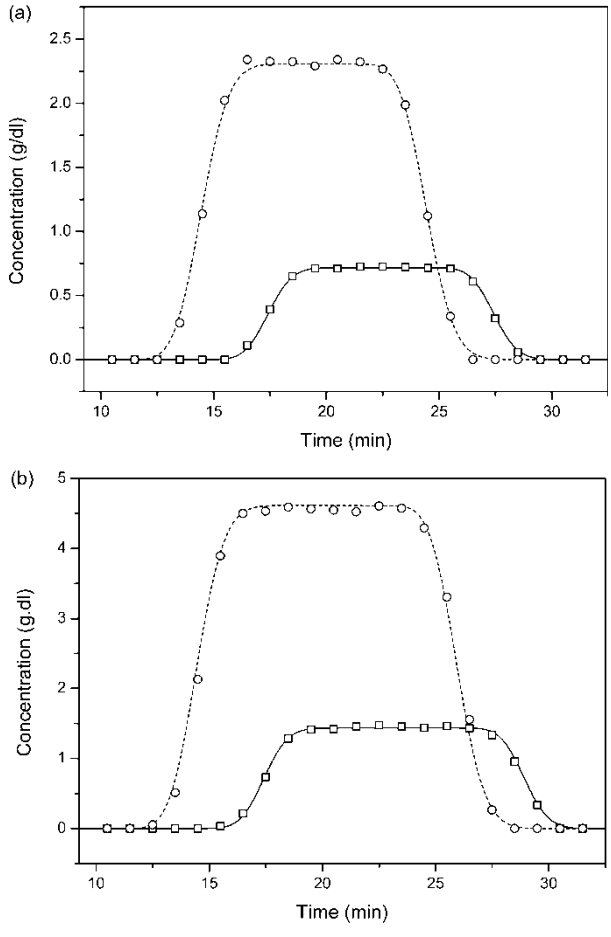

Figure 3. The comparison of experimental and simulated elution profiles of (a) Run 1, (b) Run 2, (c) Run 3, (d) Run 4, (e) Run 5, and (f) Run 6. Lines are the simulated elution profiles and open symbols are the experimental elution profiles. Solid line and square symbol are for xylitol and dash line and circle symbol are for maltitol.

(*continued*)

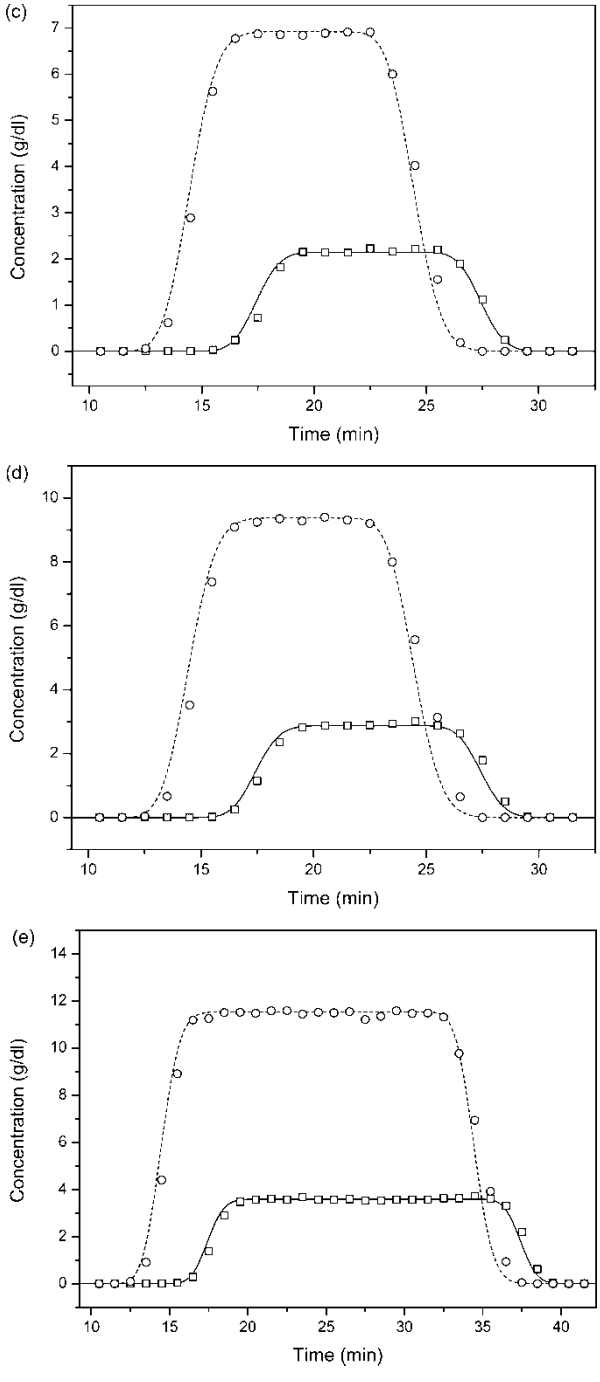

Figure 3. Continued.

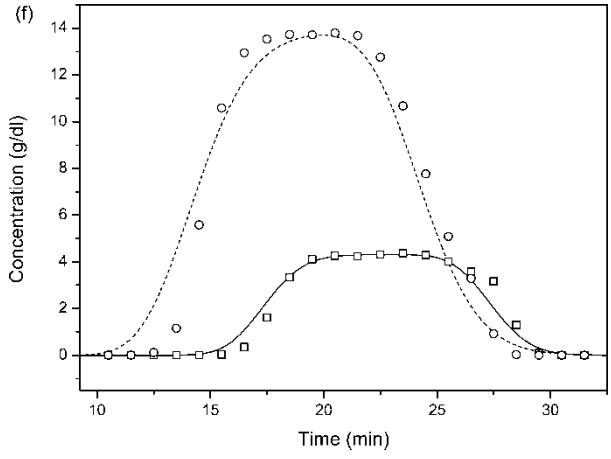

Figure 3. Continued.

is suggested. The criterion of the SMB process is $<95\%$ yield and $<95\%$ purity of xylitol and maltitol. We considered the traditional SMB process, 4 zones and 8 columns. Before determining the operating condition, the column length must be fixed. Therefore, 4 column lengths (10 cm, 15 cm, 20 cm, and 30 cm) are considered. Table 3 shows the operating conditions

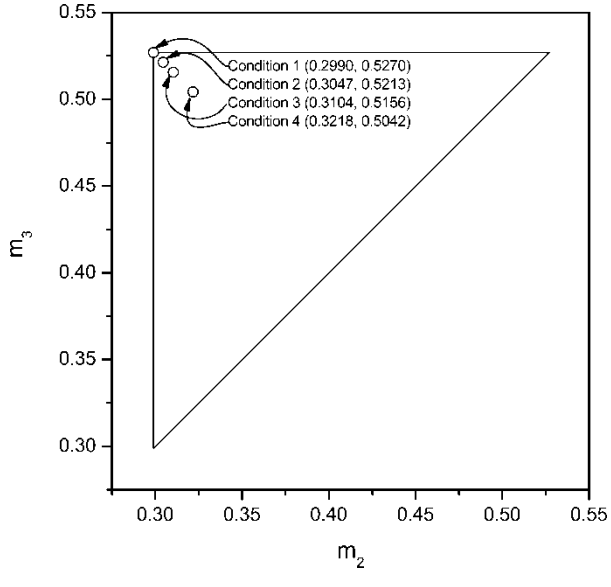

Figure 4. The m2-m3 plane of the triangle theory. The triangle region describes the separation zone. Condition 1 is vertex point and Condition 2, 3, and 4 are moved into 5%, 10%, and 20% of height of the vertex point.

Table 3. The operating conditions with various column length

	Column length (cm)	Conditions	Feed (mL/min)	Eluent (mL/min)	Raffinate (mL/min)	Extract (mL/min)	Recycle (mL/min)	Switching time (min)
Run 1	10 cm	Condition 1	0.500	0.500	0.500	0.500	2.449	1.97
Run 2		Condition 2	0.500	0.526	0.513	0.513	2.579	1.87
Run 3		Condition 3	0.500	0.556	0.528	0.528	2.723	1.77
Run 4		Condition 4	0.500	0.625	0.563	0.562	3.057	1.58
Run 5	15 cm	Condition 1	0.500	0.500	0.500	0.500	2.447	2.96
Run 6		Condition 2	0.500	0.526	0.513	0.513	2.576	2.81
Run 7		Condition 3	0.500	0.556	0.528	0.528	2.721	2.66
Run 8		Condition 4	0.500	0.625	0.563	0.562	3.064	2.36
Run 9	20 cm	Condition 1	0.500	0.500	0.500	0.500	2.449	3.94
Run 10		Condition 2	0.500	0.526	0.513	0.513	2.579	3.74
Run 11		Condition 3	0.500	0.556	0.528	0.528	2.719	3.55
Run 12		Condition 4	0.500	0.625	0.563	0.562	3.062	3.15
Run 13	30 cm	Condition 1	0.500	0.500	0.500	0.500	2.449	5.91
Run 14		Condition 2	0.500	0.526	0.513	0.513	2.576	5.62
Run 15		Condition 3	0.500	0.556	0.528	0.528	2.721	5.32
Run 16		Condition 4	0.500	0.625	0.563	0.562	3.060	4.73

to determine the column length. Figure 5 shows the result of 16 simulations (Table 3), (a) 10 cm of column length, (b) 15 cm of column length, (c) 20 cm of column length, and (d) 30 cm of column length. We already set the criterion to $<95\%$ of purity and yield of product. Table 4 shows the enrichment of products with various conditions and column lengths. The enrichments are not changed with the column length, only with operating conditions. Condition 1 (vertex point) has highest enrichments of products,

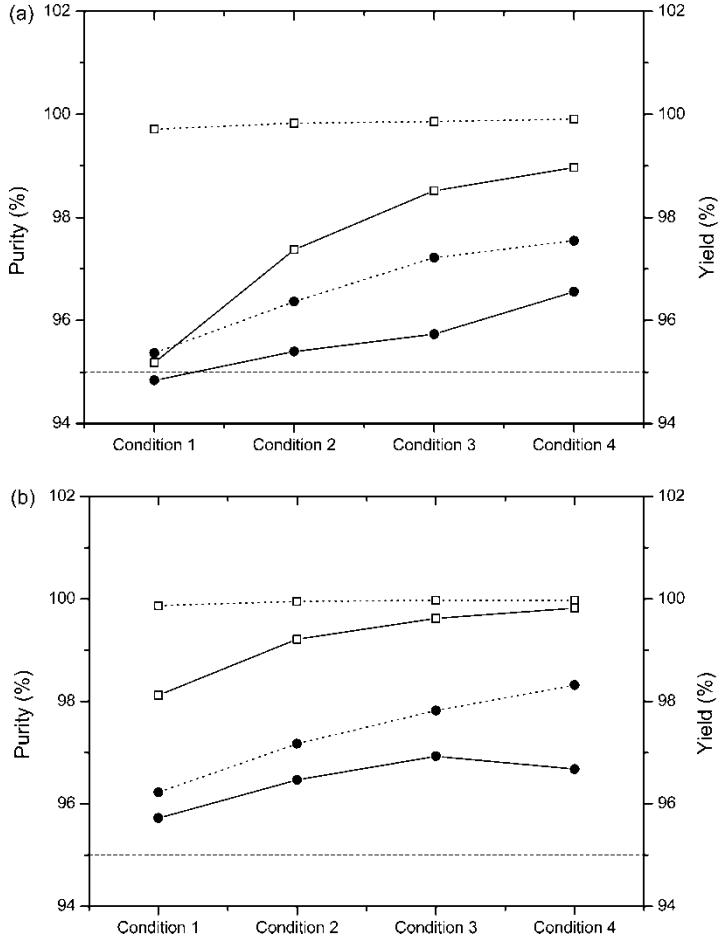

Figure 5. The result of 16 simulations (Table 3), (a) 10 cm of column length, (b) 15 cm of column length, (c) 20 cm of column length, and (d) 30 cm of column length. Open square is purity of products, closed circle is yield of products, and solid lines and dotted lines are for xylitol and maltitol, respectively. The dash line describes the criterion of SMB design.

(*continued*)

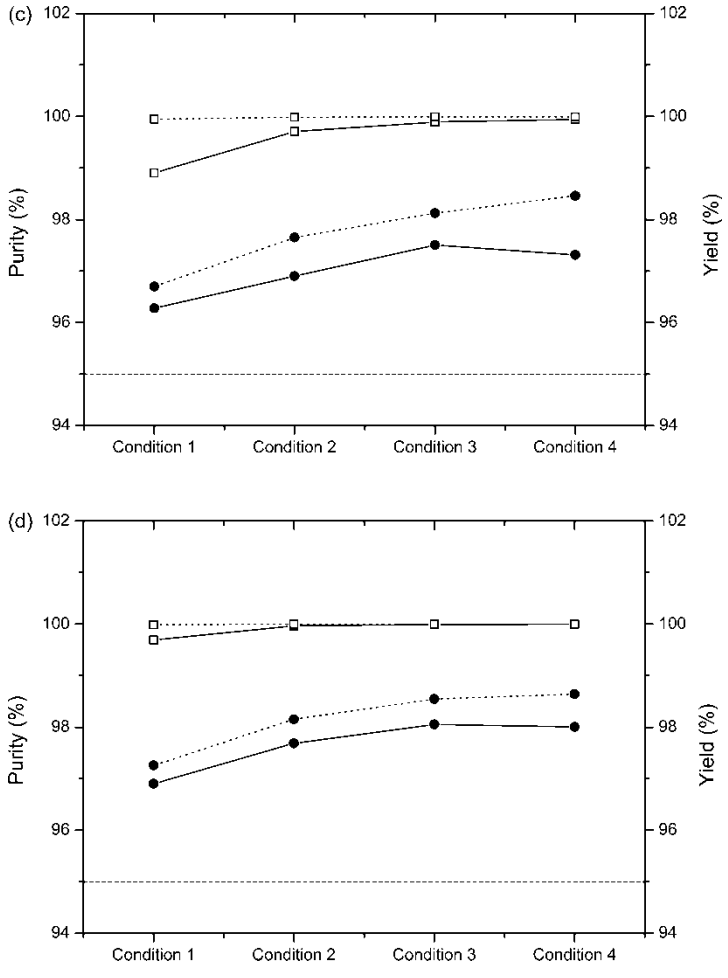

Figure 5. Continued.

so Condition 1 is optimum condition. Therefore, without sensitivity analysis, the optimum column length is 15 cm, and the optimum operating condition is Condition 1 (Run 5, Table 3).

Sensitivity Analysis

The feed concentrations are considered as the sensitivity analysis. In the light of the adsorption isotherm, these samples (xylitol and maltitol) are the linear adsorption isotherm. So, in spite of an increase in the feed concentrations, the axial dispersion coefficients are increased as feed concentrations are

Table 4. The enrichment of products

	Condition 1		Condition 2		Condition 3		Condition 4	
	Xylitol	Maltitol	Xylitol	Maltitol	Xylitol	Maltitol	Xylitol	Maltitol
10 cm	0.948	0.954	0.93	0.939	0.906	0.921	0.859	0.866
15 cm	0.957	0.962	0.94	0.947	0.918	0.926	0.86	0.873
20 cm	0.963	0.967	0.944	0.952	0.923	0.929	0.866	0.874
30 cm	0.969	0.972	0.952	0.957	0.929	0.933	0.872	0.876
Average	0.959	0.964	0.942	0.949	0.919	0.927	0.864	0.872
S.D.	0.009	0.008	0.009	0.008	0.009	0.006	0.006	0.004

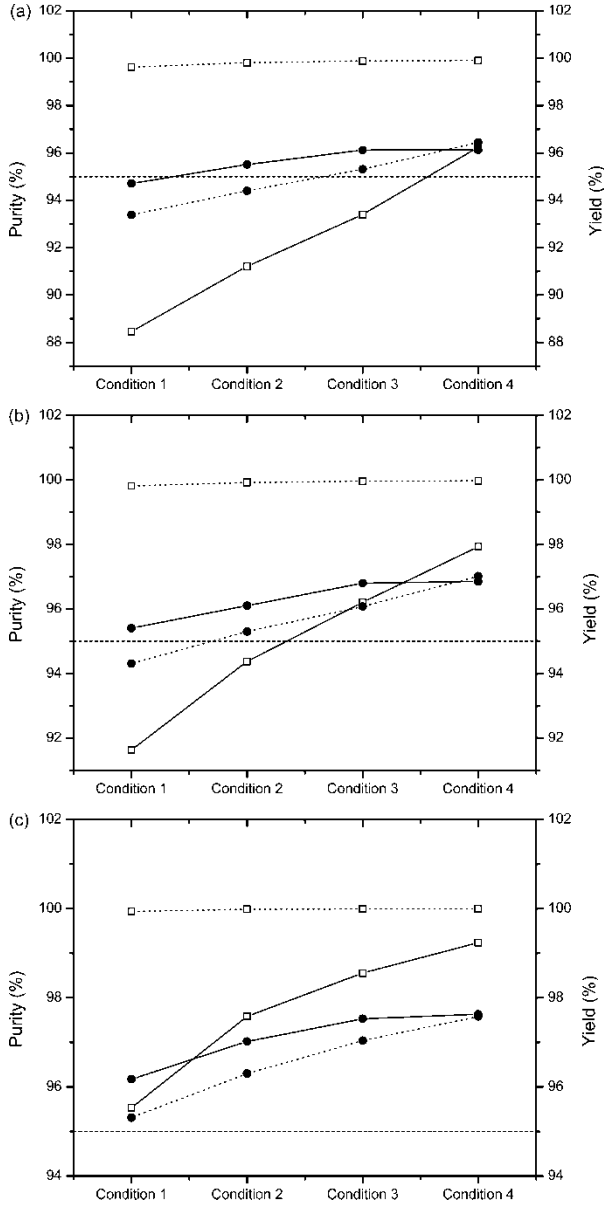

Figure 6. The result of sensitivity analysis for three SMB simulations (Table 3), (a) 15 cm of column length, (b) 20 cm of column length, and (c) 30 cm of column length. Open square is purity of products, closed circle is yield of products, and solid lines and dotted lines are for xylitol and maltitol, respectively. The dash line describes the criterion of SMB design.

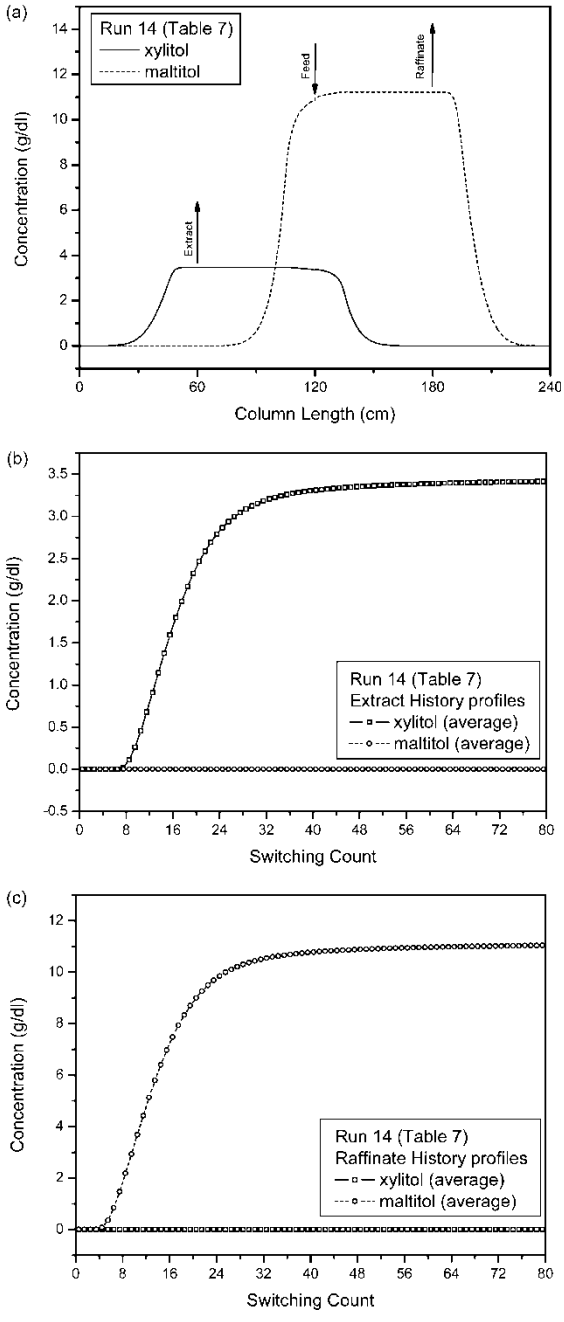

Figure 7. The column internal profiles and history profiles of extract and raffinate port of Run 14, (a) is the column internal profiles, (b) and (c) are history profiles of extract and raffinate port, respectively.

Table 5. The optimum operating conditions and instrument requirements

Operating conditions		Results	
Feed conc. (g/dL)		Purity (%)	
xylitol	3.587	Xylitol	99.965
maltitol	11.54	Maltitol	99.998
Flow rates (mL/min)		Yield (%)	
Feed	0.500	Xylitol	97.682
Eluent	0.525	Maltitol	98.150
Raffinate	0.513	Enrichment	
Extract	0.513		
Recycle	2.576		
Switching time (min)	5.62		
		Xylitol	0.952
		Maltitol	0.957

increased. There is a 20% higher range of feed concentration. Figure 6 shows the result of SMB simulation using the 20% higher feed condition (Run 6, Table 1). The three conditions (Run 8, Run 11, and Run 14; Table 3) are selected for reasonable optimum condition. The advantage of Run 8 is minimum column volume (i.e., minimum resin consumption). The advantages of Run 14 are maximum enrichments and minimum solvent consumption. Run 11 is the moderate operating condition between Run 8 and Run 14. In our opinion, Run 14 has more advantages than Run 8. Figure 7 shows the internal profiles and history profiles of the extract and raffinate port of Run 14. The operating conditions and the results of SMB simulation are listed in Table 5.

CONCLUSION

The isotherm parameters and axial dispersion coefficients of xylitol and maltitol are estimated by the frontal analysis method and iterative simulation, respectively. The isotherm of xylitol and maltitol are linear according to the anion exchange resin as the stationary phase. The SMB process for separation of xylitol and maltitol is designed and simulated based on the Triangle theory and the Equilibrium-Dispersion model. To decide the column length, several simulations were carried out with several column lengths. When a long column is used, the optimum operating condition is reached at the vertex point of the triangle separate region. Current SMB design methods are based on the ideal models that are not considered about kinetic mass transfer, such as axial dispersion coefficient and mass transfer coefficient. As the limitation of SMB design methods, the process must be designed

with an iterative simulation method in some fixed column length. As a result, the optimum column length to separate xylitol and maltitol with DOWEX 1X4 anion exchange resin is 30 cm and the operating condition is decided with a 5% safety margin in the triangle separation region.

ABBREVIATIONS

A	well retained solute
B	less retained solute
c_i	the concentration of I solute in the mobile phase
D_i	the axial dispersion coefficient of i solute
F	the phase ratio, $= (1 - \varepsilon)/\varepsilon$
H_i	the Henry's constant of I component
m_i	the flow rate ratio of zone i
Q_i	the volumetric flow rate of the liquid phase in zone i
Q_s	the volumetric flow rate of the solid phase
q_i	the concentration of I solute in the stationary phase
u	the intersticial flow rate of mobile phase
ε	the total void fraction
ε_p	the intraparticle void fraction

ACKNOWLEDGMENT

This study was supported by the ERC for Advanced Bioseparation Technology, KOSEF.

REFERENCES

1. Kwon, D.-H.; Kim, M.-D.; Lee, T.-H.; Oh, Y.-J.; Ryu, Y.-W.; Seo, J.-H. Elevation of glucose 6-phosphate gehydrogenase activity increases xylitol production in recombinant saccharomyces cerevisiae. J. Mol. Catal. B: Enzym. **2006**, *43*, 86–89.
2. Sampaio, F.C.; Faver, D.D.; Mantovan, H.C.; Passos, F.M.L.; Perego, P.; Converti, A. Use of response surface methodology for Optimization of Xylitol Production by the new yeast strain debaryomyces hansenii UFV-170. J. Food Eng. **2006**, *76*, 376–386.
3. Lee, J.W.; Lee, C.H.; Koo, Y.-M. Sensitivity analysis of amino acids in simulated moving bed chromatography. Biotechnol. Bioproc. E. **2006**, *11*, 110–115.
4. Mazzotti, M.; Storti, G.; Morbidelli, M. Optimal operation of simulated moving bed units for nonlinear chromatographic separations. J. Chromatogr. A **1997**, *769*, 3–24.
5. Wu, D.-J.; Ma, Z.; Wang, N.-H.L. Optimization of throughput and desorbent consumption in simulated moving-bed chromatography for paclitaxel purification. J. Chromatogr. A **1999**, *855*, 71–89.

6. Navarro, A.; Caruel, H.; Rigal, L.; Phemius, P. Continuous chromatographic separation process: simulated moving bed allowing simultaneous withdrawal of three fractions. J. Chromatogr. A **1997**, *770*, 39–50.
7. Tanaka, K.; Ohta, K.; Fritz, J.S. Ion-exclusion chromatography of ethanolamines on an anion-exchange resin by elution with polyols and sugars. J. Chromatogr. A **1996**, *739*, 317–325.

Received December 19, 2006
Accepted January 30, 2007
Manuscript 6010