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A novel pseudo simulated moving bed with solvent gradient for ternary separations

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ABSTRACT

A novel pseudo simulated moving bed was suggested to separate a ternary mixture. A solvent gradient was created to make the solvent strength decreasing from zone II to zone III. Under suitable conditions, the least retained solute A moved forward and the most retained solute C moved backward in zones II and III whereas the medium retained solute B moved forward in zone II but backward in zone III to be trapped in the two zones consequently. Once the columns in zones II and III were saturated with solute B, the solvent dissolving the feed was introduced at the feed port to remove solute A from the raffinate-port and solute C from the extract-port. Finally, solute B was recovered from the extract port by stopping the liquid flow in zone II. This scheme was validated by the successful separation of dihydrocapsaicin from capsaicinoids.

1. Introduction

Simulated moving bed (SMB) is a continuous chromatographic separation technique [1–4]. It consists of many columns connected to each other in a circle, and four inlet/outlet ports of the feed, raffinate, desorbent and extract divide it into four zones. The periodic switches of the four ports in the direction of the liquid flow cause the apparent counter-current movement of the solid against the liquid, and thus the least retained solute moves forward with the liquid while the most retained solute moves backward with the solid. As a result, a binary mixture can be continuously separated into two fractions flowing out of the raffinate-port and the extract-port, respectively.

However, in some cases the desired product has to be purified by eliminating impurities eluted both before and after it, which is beyond the ability of a single standard four-zone SMB. Some modifications should be given. First, a five-zone SMB is adopted to collect the medium retained solute from a side stream [5–8], or a four-zone SMB is adopted to collect the medium and the most retained solutes flow from the extract-port orderly [9–11]. Second, a cascade of two SMBs in series, which may be either separated [12,13] or combined in a single device [14,15], can also produce the medium retained component. The third modification adopts a pseudo-SMB [16–18], where the feed is discontinuously added only during a part of the total cycle time operating in a batch chromatographic mode. During the remaining cycle time, the system is operated in a SMB mode but without feeding. The last modification is a continuous, counter-current multi-column chromatographic processes incorporating modifier gradients (MCSPG process) [19–21]. Under optimal operating conditions, all the four modified schemes can produce the medium retained solute with a high purity.

In this work, we propose a novel operating mode of the SMB for ternary separations. The least and most retained solutes are first separated from the raffinate and extract stream, respectively. Meanwhile, the medium retained solute moves backward in zone III but forward in zone II by introducing a solvent gradient [22–24]. It seems that the medium retained solute is trapped. Then, the trapped solute is recovered by changing the flow rate or solvent strength in zones II and III. For the time being, we named this separation scheme as a pseudo-SMB since the separation process is not continuous.

2. Description of the pseudo-SMB

The migration velocity of a solute in a column during each switch interval is dependent on both the flow rate and the solvent strength of the liquid. In the case of isocratic elution, a solute normally moves in zone III quicker than in zone II. After switching the columns, the solute moves in the same direction in both zones II and III, either forward or backward. If the solvent strength of the liquid in zone II is higher than that in zone III, however, the solute will move faster in zone II than in zone III during each switch interval. As a result, the

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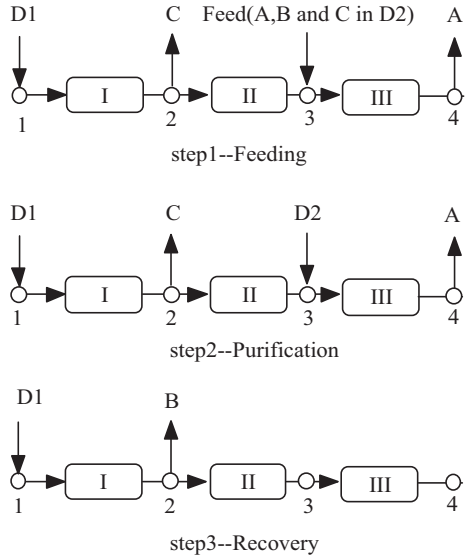

Fig. 1. Scheme of the novel pseudo-SMB for ternary separations.

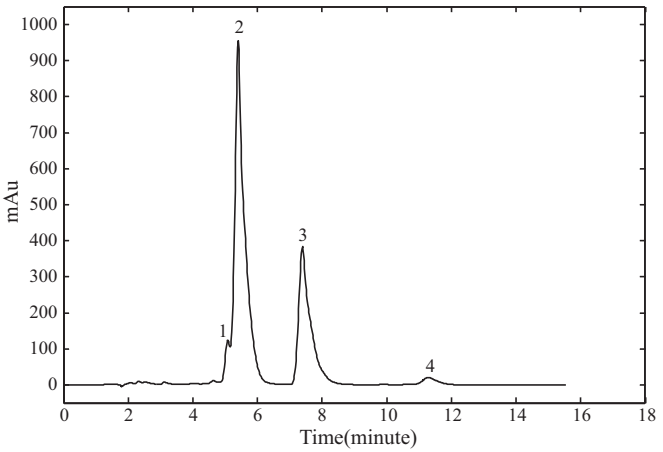

Fig. 2. The chromatogram of capsaicinoids on the ODS column using the mobile phase of methanol/water (70/30, v/v) at 280 nm and the flow rate of 1 mL/min. Components 1–4 are nordihydrocapsaicin, capsaicin, dihydrocapsaicin and homodihydrocapsaicin, respectively.

Table 1
The movement of solutes A–C in the pseudo-SMB.

Step	Solute	Zone I	Zone II	Zone III
1st	A		→	→
	B		→	←
	C	→	←	←
2nd	A		←	→
	B		←	←
	C	→	←	←
3rd	B	→	←	←

solute moves forward in zone II but backward in zone III due to the column switching, so that the solute seems to be trapped in zones II and III. The phenomenon, a little similar to the focusing effect in the liquid thermal adsorption systems [25,26], is the principle of the novel SMB operating mode, in which the medium retained solute is trapped in zones II and III and thus is separated from a ternary mixture.

Fig. 1 shows the separation process of three steps, where letters A, B and C denote the least, medium and most retained solutes in a ternary mixture, respectively and a solvent gradient is created in zones II and III along the liquid flowing direction.

- *Step 1: feeding*—The feed consisting of solutes A–C are dissolved in solvent D2, and then the solution is added at the node between zones II and III. Meanwhile, other solvent D1 is added to zone I. The solvent strength of D1 is higher than that of D2. According to the separation principle, solute A moves forward and solute C moves backward in zones II and III, while solute B moves forward in zone II and backward in zone III. That is to say, only solute B is trapped in zones II and III. Once the columns in zones II and III are saturated with solute B, feeding should be stopped to prevent the solute from leaking out of the raffinate-port.
- *Step 2: purification*—The feed is replaced to solvent D2 without changing the other operating conditions. Solutes A and C remaining in zones II and III are removed to purify solute B trapped in zones II and III.
- *Step 3: recovery*—After solutes A and C are removed completely, solute B trapped in zones II and III is recovered from the extract-port by stopping the liquid flow in zone II. As the recovery step finishes, a new feeding can be restarted.

Table 1 illustrates the movement of solutes A–C during three steps. Based on the above analyses, the key point is the solvent strength of the liquid in zone II is higher than that of the liquid in zone III. Zone IV can be added to reduce the solvent consumption, but the productivity will be increased accordingly. In this work, we adopt the three-zone SMB as shown in Fig. 1.

3. Materials and instruments

Capsaicinoids with a purity of 95% was obtained from Bis-Biotech Co. Ltd, Zhengzhou, China. It contains nordihydrocapsaicin, capsaicin, dihydrocapsaicin and homodihydrocapsaicin as shown in Fig. 2 [27]. Nordihydrocapsaicin and capsaicin are called as solute A, dihydrocapsaicin as solute B, and homodihydrocapsaicin as solute C, respectively. The solvent, methanol, was purchased from Sinopharm Chemical Reagent Co., Ltd, Shanghai, China, and the double distilled water was prepared in the laboratory.

The SMB unit consists of zones I, II and III with 2, 3 and 3 columns respectively. The columns (100 mm × 10 mm) were packed with ODS silica gel (diameter 20–45 μm, pore volume 0.83 mL/g, Fuji, Japan) following a slurry-packing technique at a pressure of 25 MPa. A mixture of methanol/water was used as the mobile phase in SMB. Two HPLC pumps (K501, Knauer, Germany) control the flow rates in zones I and II, respectively, and the third pump (P230, Elite, China) is used for feeding. As shown in Fig. 3, there are five (8 + 1)-port multiposition valves (EMT-6CSD8UW, Vici-valco, Switzerland) connected to 8 columns to control the positions of the desorbent, extract, feed and raffinate ports, respectively. The solution from zone I flows through valve 4 and then is divided into two streams: one is pumped into zone II through valve 5 and the other flows out of the system as the extract stream. A check valve is set between every two columns to prevent the liquid from backflushing. A program provided by Vici-valco is used to control the switches of the valves.

Samples from the raffinate-port and the extract-port were analyzed with a HPLC system (K501 pump, K2501 UV detector, Knauer, Berlin, Germany) at 280 nm using an ODS column (150 mm × 4.6 mm, Elite, Dalian, China) with the mobile phase of methanol/water (70/30, v/v) and the flow rate was 1.0 mL/min.

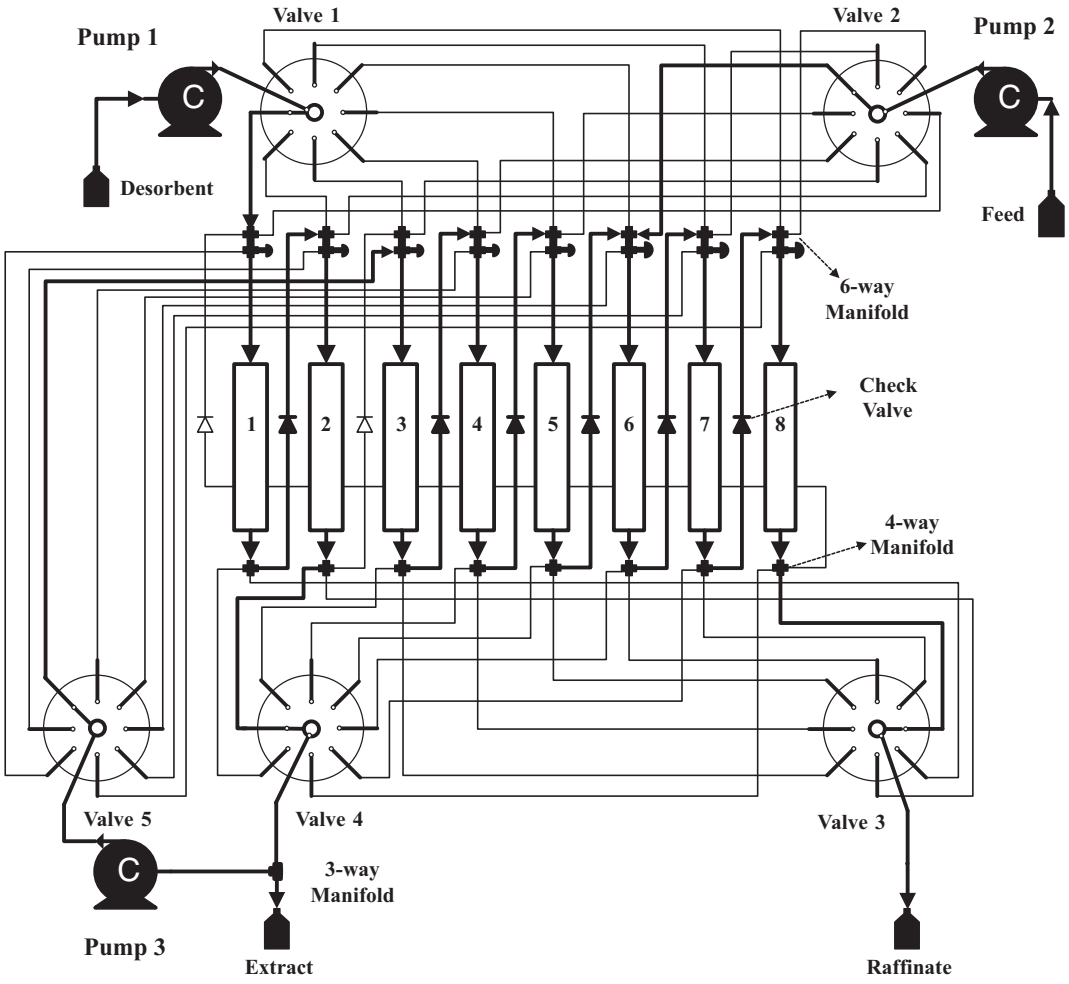

Fig. 3. Scheme of the experimental SMB laboratory unit.

4. Designing the pseudo-SMB

Table 1 provides the design criterions for operating conditions in steps 1 and 2, which can be expressed as follows:

$$w_{C,I} \cdot \Delta t \geq L \tag{1a}$$

$$w_{C,II} \cdot \Delta t \leq L \tag{2a}$$

$$w_{A,III} \cdot \Delta t \geq L \tag{3a}$$

$$w_{B,II} \cdot \Delta t \geq L \tag{4a}$$

$$w_{B,III} \cdot \Delta t \leq L \tag{5a}$$

where $w_{i,j}$ is the moving velocity of the front or tail of solute i in zone j, Δt the switch interval and L the column length. In the case of a linear adsorption [28–30], $w_{i,j}$ is:

$$w_{i,j} = \frac{F_j}{\pi \cdot (d^2/4) \cdot (\varepsilon + (1-\varepsilon) \cdot H_i)} \tag{6}$$

where d is the column diameter, ε the column voidage, F_j the volumetric flow rate in zone j, and H_i the Henry's constant of solute i. Substituting Eq. (6) into inequalities (1a)–(5a) gives:

$$F_I \cdot \Delta t > V_{R,C,I} \tag{1b}$$

$$F_{II} \cdot \Delta t < V_{R,C,II} \tag{2b}$$

$$F_{III} \cdot \Delta t > V_{R,A,III} \tag{3b}$$

$$F_{II} \cdot \Delta t > V_{R,B,II} \tag{4b}$$

$$F_{III} \cdot \Delta t < V_{R,B,III} \tag{5b}$$

where $V_{R,i,j}$ is the retention volume of solute i on the column in zone j. The retention volume is related to the Henry's constant as follows:

$$\begin{aligned} V_{R,i,j} &= V_0 \cdot (k'_{i,j} + 1) \\ &= V_{col} \cdot \varepsilon \cdot \left(\frac{1-\varepsilon}{\varepsilon} \cdot H_{i,j} + 1 \right) \\ &= V_{col} \cdot [(1-\varepsilon) \cdot H_{i,j} + \varepsilon] \end{aligned} \tag{7}$$

The value of $V_{R,i,j}$ is the volume of the liquid entering the column between the feed introduction and the emergence of the peak, and can be measured with a batch chromatography. The retention volume is dependent on the composition of the liquid in the jth zone and can be evaluated using the following empirical formula [23]:

$$V_{R,i,j} = \frac{a_i}{(1 - b_i \cdot X_j)^{c_i}} \tag{8}$$

where X_j is the water content in zone j. X_j changes periodically [23] and can be treated simply as [24]:

$$X_I = X_{II} = X_{D1} \tag{9}$$

$$X_{III} = \frac{X_{D1} \cdot F_{II} + X_{D2} \cdot (F_{III} - F_{II})}{F_{III}} \tag{10}$$

From the above inequalities and equalities, the operating conditions can be properly designed by using a procedure as shown in

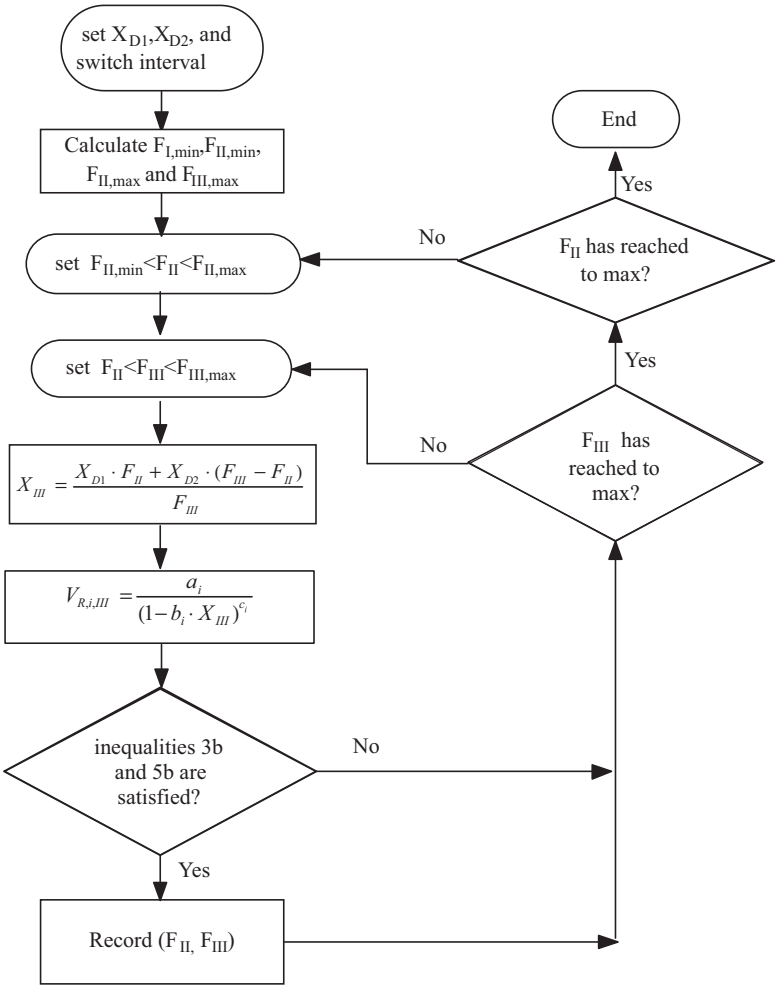

Fig. 4. Procedure to design the operating condition of the novel SMB.

Table 2
Values of *a*, *b* and *c* in Eq. (7) for solutes A, B and C.

Solute	*a*	*b*	*c*
A	4.158	3.926	3.455
B	1.779	1.559	1.205
C	2.483	3.455	6.613

Fig. 4. Firstly, the ranges of F_{II} and F_{III} are determined. The maximum and minimum of F_{II} can be obtained from inequalities (2b) and (4b) once X_{D1} and Δt are set. For F_{III}, the minimum is F_{II}, and the maximum can be calculated from inequality (5b) by substituting $X_{III,min} = X_{D2}$ into equality 7. Secondly, the sets of F_{II} and F_{III} in their range are screened to meet inequalities (3b) and (5b).

In this work, the water content in solvent D1 and D2 are 20% and 40% respectively. Fig. 5 shows the effect of the water content on the retention volume. The values of *a*, *b* and *c* are listed in Table 2. The procedure illustrated in Fig. 4 gives a separation region in the plane of $F_{II}\Delta t$ and $F_{III}\Delta t$ as shown in Fig. 6, which is actually the complete separation region in the framework of Triangle Theory [31–33]. Two points in the region were selected and the detailed operating conditions are listed in Table 3. As solute B trapped in zones II and III is gradually accumulated to increase the concentration, the assumption of the linear adsorption is not reasonable. However, the experimental results show that the design method provides a good initial guess.

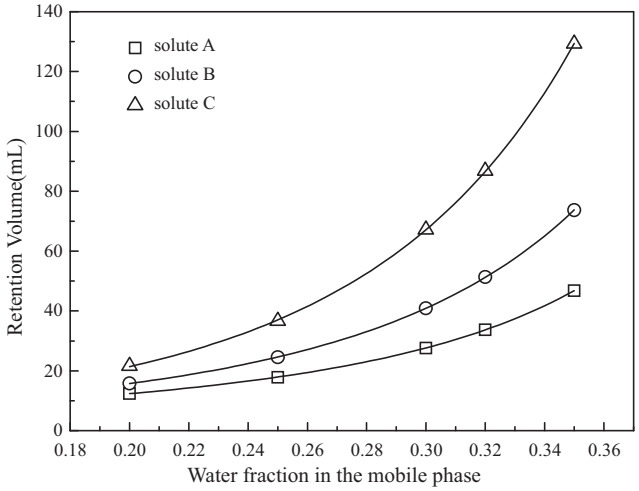

Fig. 5. The effect of the water content on the retention volume of solutes A–C.

5. Results and discussions

5.1. The feasibility of the separation process

In run 1, the raffinate and extract streams were regularly collected and analyzed. The feeding lasted for 14 switches (84 min). The result showed that during switches 1–12, solute A flowed out

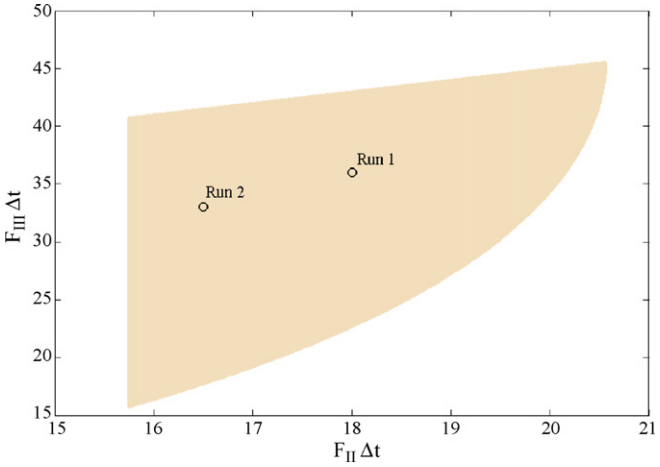

Fig. 6. Separation region in the plane of $F_{II}\Delta t - F_{III}\Delta t$.

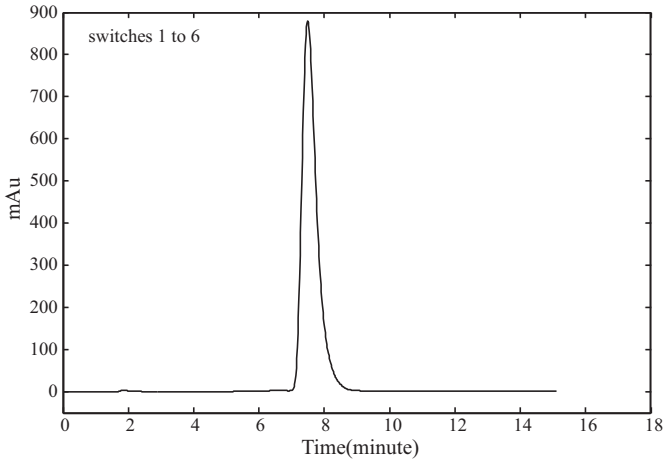

Fig. 7. Chromatogram of the extract stream during step 3 in run 2. The chromatographic conditions are identical to those applied in Fig. 2.

Table 3
Operating conditions in runs 1 and 2.

	Δt (min)	F_I (mL/min)	F_{II} (mL/min)	F_{III} (mL/min)	C_{Feed} (g/L)
Run 1					
Step 1	6	4.5	3.0	6.0	20
Step 2	6	4.5	3.0	6.0	–
Step 3	6	3.0	0	0	–
Run 2					
Step 1	5.5	4.5	3.0	6.0	20
Step 2	5.5	4.5	3.0	6.0	–
Step 3	5.5	3.0	0	0	–

of the raffinate-port and solute C from the extract-port respectively, and there was no solute B flowing out of zones II and III. However, solute B started to leak out of zone III during switches 13–14 with circa time from 72 to 84 min. We may call the time of solute B leaking out of zone III in the feeding duration as the leakage point.

In the follow-up purification step, the feed solution was displaced by the solvent D1 without changing the other operating conditions. As solute B had leaked in the feeding duration, the raffinate stream during switches 1–8 in the purification duration contained solute B. After about 24 switches for about144 min, solutes A and C were removed completely. Then the purified solute B could be easily eluted out of the system. The experiments showed that if we stopped the flow in zone II, and reduced F_I from 4.5 mL/min to 3.0 mL/min, the recovery of solute B from zones II and III containing 6 columns was completed right after 6 switch intervals, and the extract stream in the third step contained solute B only. The detailed separation performances such as the recovery (R), the productivity (P) and the solvent consumption (S) are listed in Table 4. The three indexes were calculated as follows:

$$R = \frac{C_{B,R} \cdot F_{D1,R} \cdot \Delta t \cdot n_R}{C_{B,Feed} \cdot F_{Feed} \cdot \Delta t \cdot n_F} \quad (11)$$

$$P = \frac{C_{B,R} \cdot F_{D1,R} \cdot \Delta t \cdot n_R}{(V_{col} \cdot N_{col}) \cdot (\Delta t \cdot (n_F + n_P + n_R))} \quad (12)$$

$$S = \frac{(F_{Feed}+F_{D1,F}) \cdot \Delta t \cdot n_F + (F_{D2,P}+F_{D1,P}) \cdot \Delta t \cdot n_P + F_{D1,R} \cdot \Delta t \cdot n_P}{C_{B,R} \cdot F_{D1,R} \cdot \Delta t \cdot n_R} \quad (13)$$

where $C_{B,Feed}$ and $C_{B,R}$ are the concentration of solute B in the feed solution and the extract stream collected in step 3 respectively, $F_{D1,F}$, $F_{D1,P}$ and $F_{D1,R}$ are the flow rates of solvent D1 in steps 1–3, F_{Feed} is the feeding rate in step 1, $F_{D2,P}$ is the flow rate of solvent D2 in step 2, and n_F, n_P and n_R are the number of switches in steps 1–3. The recovery of solute B

Table 4
Separation performances of runs 1 and 2.

	Run 1	Run 2
Feeding duration (min)	84	88
Leakage point (min)[a]	72–84	Without leakage
Purification duration (min)	144	132
Recovery duration (min)	36	33
Feed amount (g)	4.79	5.02
Purity (%)	100	100
Recovery (%)	91.0	100
Solvent consumption (L/g)	1.43	1.19
Productivity (g/L/h)	4.89	5.38

[a] Leakage point is the time of solute B starting to leak out of zone III in the feeding duration.

was 91% due to a little leakage in the feeding and purification duration.

The result confirms the feasibility of the novel operating mode of the SMB with a solvent gradient for the separation of the medium retained solute from a ternary mixture. However, it seems that solute B leaks too early in the feeding step, and thus, an attempt was made to reduce the switch interval for prolonging the feed duration.

5.2. The effect of switch interval on the feeding duration

In run 2, the switch interval was reduced from 6 to 5.5 min so as to increase the simulated countercurrent movement of solute B in zones II and III. The feeding duration is 16 switches (88 min) and solute B did not leak out of zone III. In comparison with run 1, it was suggested that the effective feed duration without the leakage of solute B should be increased from 72 min to 88 min at least. In step 2 with 24 switches, solutes A and C were completely removed from the raffinate and extract ports respectively. In step 3, pure solute B was obtained during 6 switches as shown in Fig. 7. As no solute B leaked in steps 1 and 2, the recovery, the productivity and the solvent consumption were superior over those given by run 1 as listed in Table 4.

The operating mode provides a new idea for ternary separations with the SMB. However, the productivity and the solvent consumption were not very satisfactory. The key is to increase the feed duration and reduce the purification and recovery durations, which is still under research.

6. Conclusions

A novel operating mode of SMB is suggested to separate the medium retained solute from a ternary mixture consisting of the least, medium and most retained solutes (A–C). By creating a gradient of the solvent strength along the flow direction of the liquid, solute B moves forward with the liquid in zone II but backward with the switching column in zone III. For the other two solutes, there just is a binary separation process. Thus, solute B can be trapped and purified in zones II and III while solutes A and C are removed from the raffinate and extract ports, respectively.

This method separated capsaicinoids successfully. A mixture of methanol/water (80/20, v/v) was used as the desorbent, and the feed was dissolved in methanol/water (60/40, v/v). Thus, the liquid in zone II had a solvent strength higher than that in zone III so that only the medium retained solute, dihydrocapsaicin, was trapped until the columns in zones II and III were saturated. Then, the feed solution was changed to methanol/water (60/40, v/v) and the medium retained solute trapped in zones II and III was further purified through removing the least and most retained solutes. After purification, the medium retained solute was recovered from the extract port by stopping the flow in zone II.

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