A NEW PROCESS FOR MULTICOMPONENT CONTINUOUS SEPARATION BY COMBINING MULTIPLE LIQUID CHROMATOGRAPHY COLUMNS

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As a method for making liquid chromatography a continuous operation, a simulated moving-bed adsorber has been applied. This method is applicable only to two-component mixtures. Hence a new process for multi-component separation by combining multiple liquid chromatography columns was proposed. Its applicability was confirmed partly by experiments with a single column in the process and partly by simulation of the separation of dimethyl phthalate, diethyl phthalate, and di-*n*-butyl phthalate. The results showed that a mixture of more than three components can be separated and refined by use of this process. The values of distribution coefficient and overall mass transfer coefficient for each component required for the simulation were obtained from impulse response experiments, using the same column.

Introduction

Liquid chromatography has been used in many fields for analysis of various components in a mixture. It is now being used also for mixture separation. The mixture to be separated into its components is injected at regular intervals and the components coming out of the column are checked with a UV detector or the like. Based on the results, each component is collected by using a fraction collector. This method is a semicontinuous operation and is not suitable for treating a large quantity of mixture.

Hence a simulated moving-bed adsorber was proposed as a method of continuous separation[2]. This process has actually been used on an industrial scale for separation of glucose/fructose mixture and others, and many studies of this process has been made. But this process cannot be applied when the mixture contains more than three components. Hashimoto *et al.* have suggested a process for continuous separation of mixtures with three components[3]. This process makes the separation of three components, A, B, and C, possible by alternately arranging columns of two types: one with the distribution coefficients A > B > C and the other with A > C > B. Hence the process requires two types of columns packed with different adsorbents. But it is not so easy to develop adsorbents satisfying the above condition for a given mixture. A rotating

annular chromatograph has also been developed for continuous multicomponent separation[1]. This method uses cross flow. It is generally difficult, however, to separate multiple components with high purity and high yield when this process is used.

In this study, a new process is proposed. It can continuously separate a mixture of more than three components without such conditions for the adsorbent. This is realized by combining multiple columns. The appropriateness of this process is confirmed partly by experiments on a subsystem and partly by simulation of the whole system.

1. Proposed Separation Process

1.1 Basic configuration of the process

When an n-component mixture is separated by this process, the system is composed of several column-groups each of which consists of more than $(n-1)$ columns. In this paper, a three-component separation process with recovery of desorbent is considered as an example so that the process configuration can be understood easily.

Figure 1 is a conceptual figure of its basic configuration. This system comprises four column-groups, each consisting of three columns. These column-groups are named "recovery zone", "separation zone", "refining zone" and "desorption zone", respectively, according to their role in the process.

The feed solution is supplied to the right-hand column in the separation zone, and the desorbent is supplied to each column in the refining zone and the desorption zone.
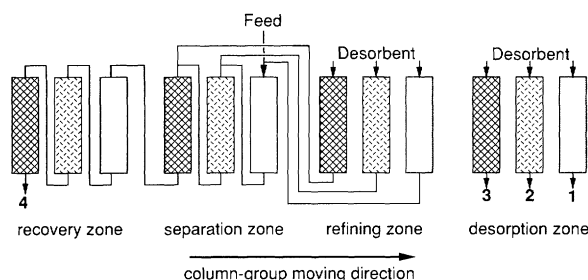
Fig. 1. Schematic representation of a multicomponent continuous separation process

As shown in Fig. 1, there are series connections between columns in the separation and recovery zones, and there are parallel connections between each column in the refining zone and the corresponding one in the separation zone. In the desorption zone, the flow in each column is independent.

1.2 Operation of this process

Let us suppose that there are three components, A, B, and C, in the feed solution where component A has the largest distribution coefficient, B the second and C the smallest.

In the process, the feed solution and the reflux solution from the right-hand column in the refining zone are fed into the right-hand column in the separation zone. Since components B and C are adsorbed more weakly than component A, both B and C flow out earlier and enter the middle column in the separation zone with the reflux solution coming from the middle column in the refining zone. In the middle column of the separation zone, since component C is adsorbed more weakly than B, component C flows out earlier and enters the left-hand column in the separation zone with the reflux solution coming from the left-hand column in the refining zone. And when component A begins to break out of the right-hand column in the separation zone or component B begins to break out of the middle column that zone, all column-groups are shifted rightward. That is, the three columns which acted as the recovery zone now become the separation zone, and those that were the desorption zone now become the recovery zone. This movement of column-groups is realized by the actual movement of all column-groups or by a change of lines connecting the columns to the direction opposite that of the movement of column-groups.

The desorbent is supplied to each column in the refining zone. Its flow rate is determined so that weakly-adsorbed components flow out in the interval between successive movements, and only the component specified to each column remains. In the right-hand column in the refining zone, for example, components B and C are adsorbed weakly and flow out comparatively earlier than A, leaving only A in the column. Of course, some A leaves the column.

The flow from this right-hand column, containing components B and C and some A is mixed with the feed solution, which contains components A, B, and C, and enters the right-hand column in the separation zone.

In the middle column in the refining zone, component C is adsorbed more weakly than B and flows out comparatively earlier, leaving only B in the column. Component C and some component B are mixed with the solution coming from the right-hand column in the separation zone, containing components B and C, and is fed into the middle column in the separation zone.

In the above example of three-component separation, only component C remains in the left-hand column in the refining zone. Hence desorbent need not be supplied to the left-hand column. When the mixture has four components, components C and D remain in the left-hand column. Then it is necessary to supply desorbent to the left-hand column in the refining zone to remove component D so that only component C remains.

The column-group with only the intended component in each column in the refining zone is then shifted to the desorption zone. In this zone, desorbent is supplied to each column, and each component is recovered from the corresponding column. Hence, each of the three components in feed solution is collected from the corresponding column in the desorption zone.

The column-group in the desorption zone is then shifted to the recovery zone. This zone adsorbs component C and prevents it from flowing out the bottom of the left-hand end of the columns in this zone. Hence pure desorbent is recovered from the left-hand column in this process.

2. Experimental

2.1 Column and solution

Experiments were made by using a column packed with silica gel (mean diameter 60 μm). The column was 20 mm in inside diameter and 100 mm long. A mixture of hexane and ethyl acetate in the ratio 3 : 2 was used as desorbent as well as the solvent in feed solution. The target mixture to be separated contained dimethyl phthalate, diethyl phthalate and di-n-butyl phthalate, in the volumetric ratio 1 : 1 : 1.

2.2 Experimental apparatus and method

a) Adsorption isotherms The adsorption isotherms for the three components described above were measured by the equilibrium desorption method at room temperature. A certain amount (5 g) of adsorbent powder was added to the solution, which was then vibrated for about 6 hours to achieve equilibrium. Then a certain volume of the solution was taken, and its quantitative analysis was made by

another column of HPLC by using a UV detector, where the wave length was set at 290 nm. Based on the observed concentration, the adsorbed amount was calculated by the mass balance of each component.

b) Impulse response $10\,\mu l$ of the target mixture described above in which each component was at 0.2 vol% concentration was injected into the column described above and the elution curve was obtained at room temperature by setting the desorbent flow rate at 3.0 ml/min.

c) Single-column experiment   An experiment on the behavior of the right-hand column in the separation zone was made at room temperature. This column was selected because all three components were observed in it and its behavior was the most complicated in this process. To simulate the behavior of this column at steady state, a program developed for the simulation of pressure-swing adsorption[4] was applied. In this study, the flow rate and temperature are assumed constant. The equations used in this simulation are summarized in **Table 1**, where linear adsorption isotherms were applied as a first-step approximation.

By using this simulator, the transient change in the concentration of each component at the entrance of the right-hand column in the separation zone was calculated. The result after the 30th movement of column-groups was used as the steady-state data. This calculated transient change in the concentration of each component was then realized by using four pumps and other facilities shown in **Fig. 2**. The flow of each pump was controlled by a computer (PC-9801VM) via RS-232C. The solution of component C1 (dimethyl phthalate), C2 (diethyl phthalate), or C4 (di-*n*-butyl phthalate) in each container was at 0.2 vol% concentration. D in Fig. 2 is the tank for desorbent.

To check the similarity between calculated and experimental results, the transient change in concentration of each component at the entrance of the column was analyzed first. Then the concentration of each component was measured by fractionating the exit solution at regular intervals and by making its quantitative analysis by HPLC described in a).

3. Experimental Results

3.1 Adsorption isotherms

The measured adsorption isotherms are shown in **Fig. 3**, where the data at low concentration are shown in detail. These curves cannot be extrapolated to higher concentration because the adsorption isotherms take a sigmoid shape when the data at higher concentration are included. The data in Fig. 3 are represented by the quadratic equations shown in the figure. The solid lines are based on those equations. It

Table 1. Basic equations

$$v\frac{\partial C}{\partial z}+\varepsilon\frac{\partial C}{\partial t}+(1-\varepsilon)m\frac{\partial C^*}{\partial t}=0$$

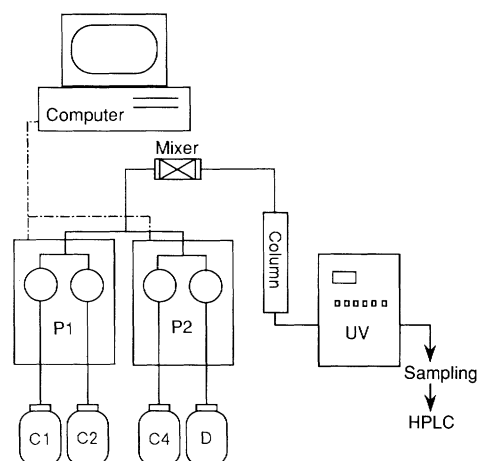$$(1-\varepsilon)m\frac{\partial C^*}{\partial t}=K_f a_v(C-C^*)$$

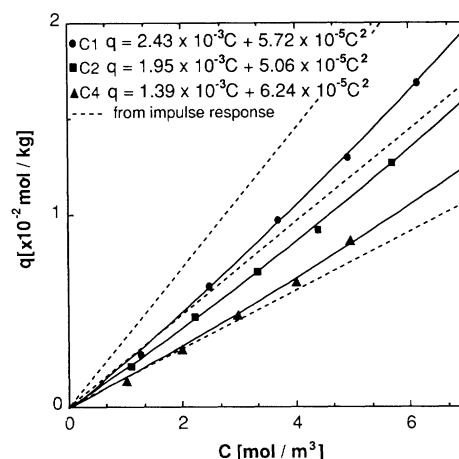**Fig. 2.** Schematic diagram of experimental apparatus used in the single-column experiment

Fig. 3. Adsorption isotherms of dimethyl phthalate, diethyl phthalate and di-*n*-butyl phthalate

is found that the isotherms for the three components are quite similar to one another and that dimethyl phthalate (denoted as C1) is adsorbed most strongly while di-*n*-butyl phthalate (denoted as C4) is adsorbed most weakly.

Based on those data, the distribution coefficients are calculated at a concentration of 0.1 vol% (i.e., $C=6.13\,\text{mol/m}^3$ for C1, $5.54\,\text{mol/m}^3$ for C2, $5.01\,\text{mol/m}^3$ for C4), which is half the concentration of each component used in the single-column experiment, and these values are shown in the m_e column in **Table 2**. For this conversion, the packed density of the adsorbent in this column is needed and is

Table 2. Properties of columns

Material	m_c [—]	m_r [—]	$K_f a_v$ [s^{-1}]
C1	1.19	1.5532	1×10^6
C2	0.955	1.0340	1×10^4
C4	0.729	0.6500	1×10^2

obtained by packing the absorbent closely in a cylindrical vessel and measuring the weight and volume of this adsorbent layer ($\rho = 0.428$ g/cm^3).

3.2 Impulse response

The experimental result for impulse response is shown in **Fig. 4(a)**, while the curve obtained by the simulation is shown in **Fig. 4(b)**. In this simulation, the distribution coefficient and the overall mass transfer coefficient for each component are required. The former was obtained from the elution time measured by the data of this impulse response, and the latter was determined so that the shape of each peak in the simulation matched that observed in the experiment. These values are summarized in the m_r and $K_f a_v$ columns in Table 2. Very large values of $K_f a_v$ were caused by using a differential axial distance as large as 0.2 mm for the adsorbent particle of average diameter 60 μm.

Comparison of Figs. 4(a) and (b) shows that these figures agreed quite well as a whole but that a slight difference is seen in the parts at low concentration, e.g., at the beginning and end of peaks. In these parts, the experimental result gives broader peaks than those by simulation. Especially, the beginning part of the di-n-butyl phthalate curve is distributed much more broadly than that by simulation, while the difference between experiment and simulation is small at the end part of dimethyl phthalate.

Based on the values of m_r in Table 2, the relations between the concentration C in solution and the adsorbed amount q per unit mass of adsorbent can be obtained. They are represented by the dashed lines in Fig. 3. Comparison of the solid curves and dashed lines in Fig. 3 or the distribution coefficients m_e and m_r in Table 2 shows that similar results were obtained for diethyl phthalate and di-n-butyl phthalate but that significant deviation was seen for dimethyl phthalate. The reason for these deviations has not yet been clarified. The distribution coefficients m_r obtained by the impulse response were used in the following simulation for the single-column experiment, since the column used in that experiment was the same as one used in the impulse-response experiment.

3.3 Single-column experiment

The transient changes in concentration of each component which were simulated for the flow at the entrance of the right-hand column in the separation
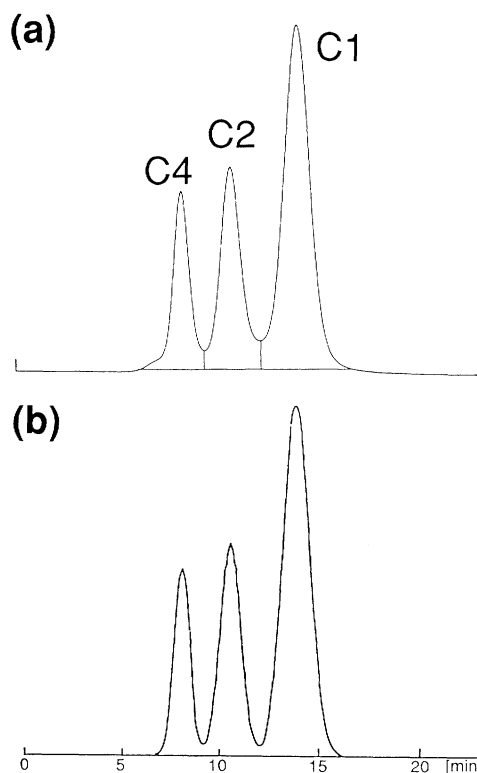

Fig. 4. Elution curves for the impulse response
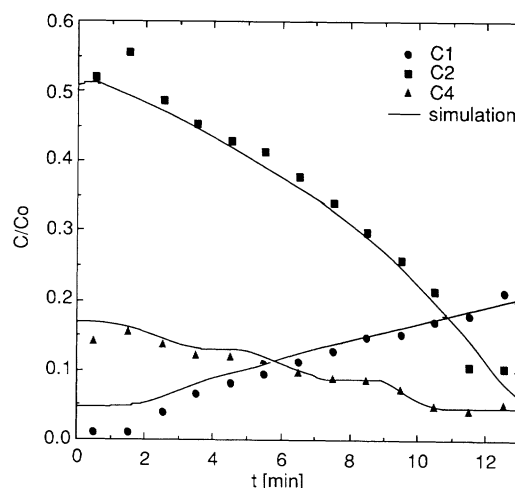(a) Experiment; (b) Simulation

Fig. 5. Transient change in concentrations at the column entrance by simulation and realized result

zone are shown by the solid lines in **Fig. 5**. This is the column into which feed solution and reflux from the right-hand column in the refining zone were introduced. The flow rates for this run are listed in **Table 3**. In this process, the operation variables are the flow rates in refining and desorption zones and the period between successive movements of the column-groups. At first, the flow rates of the right-hand and middle columns in the refining zone were determined by trial and error on the simulator, so the period was set as described in 1.2. Then the

Table 3. Flow rates

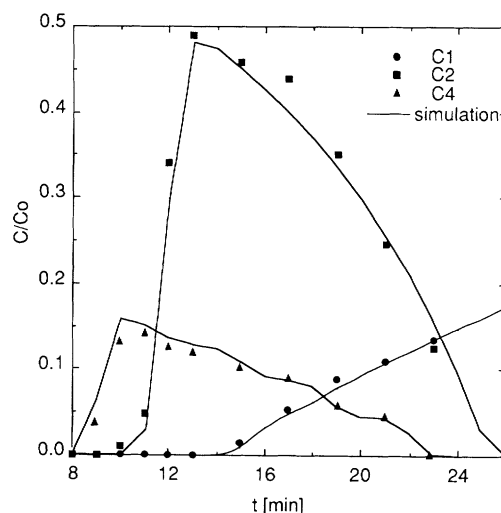|	Column 1 [ml/min]	Column 2 [ml/min]	Column 3 [ml/min]
Feed	0.12		
Desorbent 1*	2.58	1.92	0.00
Desorbent 2**	1.20	0.90	1.98

* desorbent in refining zone
** desorbent in desorption zone

appropriate flow rate in each column in the desorption zone was obtained. If the flow rates of desorbent in the refining zone are increased, the period becomes shorter. In this experiment it was set as 13 min. This is discussed in detail later. The transient changes at steady state were generated by the four pumps and are shown by closed keys in Fig. 5. It is found that transient changes in the concentration of each component are realized satisfactorily by using the experimental apparatus in Fig. 2.

For the inlet flow, the transient changes in concentration of each component at the exit of the column are shown in **Fig. 6**. Similarly to Fig. 5, the experimental data are shown by closed keys, the simulation results by curves. The stage in the separation zone continues for 13 min. Hence the latter half, i.e., the latter 13 min of the total 26 minutes, corresponds to the right-hand column in the refining zone.

In Fig. 6, di-n-butyl phthalate begins to flow out at about 8 min, and its concentration becomes maximum at around 10 min. Then it gradually decreases and at 13 min, i.e., the shift time, it remains high. The fraction that flows out before 13 min enters the middle column in the separation zone. Figure 6 shows that this fraction is nearly half the di-n-butyl phthalate fed into the column. Diethyl phthalate begins to flow out at about 10 min, and its concentration peaks at around 13 min. Hence the fraction up to this peak goes to the middle column. This is about one-eighth of the introduced diethyl phthalate. On the other hand, dimethyl phthalate is held in the column and is not detected at the column exit in this stage. So there is no loss of dimethyl phthalate.

At 13 min, all column-groups are shifted. Hence this single column is located in the refining zone. The desorbent flow rate in the refining zone is assumed as 2.58 ml/min, as shown in Table 3. But the abrupt change in total flow by the apparatus shown in Fig. 2 was difficult; therefore, the experiment after 13 min was continued by setting the inlet concentrations of the three components to zero at a total flow rate of 2.70 ml/min. Hence this desorbent flow rate is 4.4% greater than the actual one. The simulation for the latter half shown in Fig. 6 was also made for this

Fig. 6. Comparison of the experimental result of transient change in concentrations at the column exit and the simulation

higher flow rate. Since half the di-n-butyl phthalate has flowed out in the separation zone, the rest flows out before 23 min. This fraction is mixed with the feed flow and introduced to the right-hand column in the separation zone. Therefore the shape of the decreasing curve for this component is similar to that in Fig. 5. Since the reflux fraction for this component is as high as one-half, its peak in Fig. 6 is not so high. For diethyl phthalate, on the other hand, only about one-eighth had flowed out in the separation zone; thus the rest that flows out before 26 min is returned to the column in the separation zone. Hence the peak for this component in Fig. 6 becomes quite high. This shows that the concentration at the outlet of the column in the desorption zone is affected by the refluxed volume and the flow rate of desorbent in the refining zone.

Di-n-butyl phthalate and diethyl phthalate are all refluxed during the period between 13 min and 26 min, while dimethyl phthalate is held in the column. Then this column is shifted to the desorption zone and dimethyl phthalate is recovered. This desorption is done for the next 13 min. The required desorbent flow rate was simulated as 1.20 ml/min, as shown in Table 3.

Figure 6 shows that the simulation results represent the experimental data satisfactorily. Consequently, this single-column experiment shows that the performance of the total process may be determined by simulation.

3.4 Prediction of separation performance

The performance of the process shown in Fig. 1 is simulated by using the values of m_r and $K_f a_v$ shown in Table 2. Although the shift period may be determined by checking the exit concentration of columns in the separation zone, as described in 1.1, a constant shift period of 13 min was used in this case
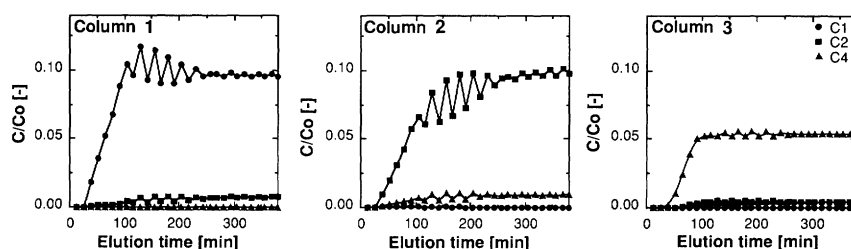
Fig. 7. Change in concentration of each component in the products taken in desorption zone

so as to simplify the operation and facilities of this process, making it more easily applicable in industry.

The flow rates for the other columns are also shown in Table 3. **Figure 7** represents the changes in average concentration for each component in the solution which flowed out of each column in the desorption zone during the shift period. Purity and recovery of each component at the final stage are shown in **Table 4**. It is found in Fig. 7 that the concentration of di-*n*-butyl phthalate is about half that of dimethyl phthalate or diethyl phthalate. This is because desorbent is not supplied to the left-hand column in the refining zone from which di-*n*-butyl phthalate is recovered. If desorbent is supplied to the column in the refining zone and the reflux flow is returned to the corresponding column in the separation zone, the concentration of di-*n*-butyl phthalate may be made much higher.

It is also noted that the process approached steady state at about 130 min (i.e., about 10 shift periods) and actually reached steady state at about 260 min (i.e., about 20 shift periods). So we may say that the process attains to steady state rather quickly.

Figure 7 and Table 4 show that each component is separated and refined satisfactorily. Hence, a three-component mixture can be continuously separated by the process proposed in this paper. It is suggested from the above discussion that higher purity and lower flow rate of desorbent may be expected by increasing the number of column-groups. This will be discussed in a future paper.

Conclusion

A new process for multicomponent continuous separation by combining multiple columns was proposed.

Separation of a mixture of dimethyl phthalate, diethyl phthalate and di-*n*-butyl phthalate was done by using as desorbent a mixture of hexane and ethyl acetate at a ratio of 3:2. An impulse response experiment gave distribution coefficients and overall mass transfer coefficients for the three components. The distribution coefficients were also calculated by the observed isotherms. But there were some differences in these two sets of distribution coefficients.

Table 4. Separation capacity

	Column 1 (C1)	Column 2 (C2)	Column 3 (C4)
Purity [%]	92.8	91.2	92.2
Recovery [%]	96.4	74.0	88.8

The transient changes in concentration of each component at the entrance of the right-hand column in the separation zone were predicted by using a simulation, and those changes were then experimentally realized by pumps to confirm the applicability of this simulation. The transient changes in concentration of each component at the column exit were measured and compared with the simulation. The agreement of experiment with simulation suggested the practicality of this process. High purity and recovery can be expected.

Nomenclature

a_v	= specific surface area	[m^2/m^3 bed]
C	= concentration in the mobile phase	[mol/m^3]
C^*	= concentration in equilibrium with the stationary phase	[mol/m^3]
K_f	= overall mass transfer coefficient	[m/s]
m_e	= distribution coefficient from adsorption isotherms	[—]
m_r	= distribution coefficient from impulse response	[—]
q	= amount adsorbed	[mol/kg]
t	= time	[s]
v	= superificial velocity of liquid flow	[m/s]
z	= axial distance	[m]
ε	= bed voidage	[—]

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