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Online publication date: 10 December 1999

To cite this Article Hu, Xien(1999) 'Recovery of Theophylline in Effluent with 2-Ethylhexanol Extraction Process', Separation Science and Technology, 34: 14, 2905 — 2922
To link to this Article: DOI: 10.1081/SS-100100812
URL: http://dx.doi.org/10.1081/SS-100100812

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SEPARATION SCIENCE AND TECHNOLOGY, **34**(14), pp. 2905–2922, 1999

Recovery of Theophylline in Effluent with 2-Ethylhexanol Extraction Process

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ABSTRACT

The 2-ethylhexanol extraction process is developed to recover theophylline in the effluent from the commercial synthesis of theophylline. The extraction of theophylline by 2-ethylhexanol depends on the pH, temperature, and Na_2SO_4 content in the effluent. The distribution ratio is 0.81 at pH 7 and decreases with increasing pH to near zero at $pH > 8$. Over 95% of the theophylline in the effluent can be recovered by 4-stage countercurrent extraction with a flow ratio equal to 2. The reciprocating plate column (RPC) was used successfully with a throughput of 3.4 t/h in the commercial process. The scaleup design was based on pilot test data and the Karr correlation. A Davy-McKee mixer-settler with sufficient resident time was used for stripping with 0.2 mol/L NaOH solution and a flow ratio of 10. After stripping, the 2-ethylhexanol was recycled for extraction. The stripping is governed by the molar ratio of NaOH in solution to theophylline in the loaded 2-ethylhexanol and by the contact time of the organic phase with the aqueous phase.

Key Words. Solvent extraction; Recovery; Theophylline; 2-Ethylhexanol

INTRODUCTION

Theophylline, 1,3-dimethylxanthine ($C_7H_8N_4O_2$, CAS 58-55-9), is usually used for the preparation of many such drugs as aminophylline, theophylline sodium glycinate, etc. In commercial production, theophylline is the parent of caffeine, which is obtained by methylation of theophylline, so that theophylline is generally produced as a by-product in the caffeine synthesis pro-

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cess (1). A large amount of theophylline remains in the mother solution after crystallization from the synthesis process, with a theophylline content of 0.5–0.7% in the solution. For example, about 12 kt/y of the solution will be released to synthesize 1 kt/y of caffeine with 84 t/y theophylline in the mother solution. Therefore, if the solution were discharged as effluent without recovery, a large amount of theophylline would be lost.

Besides theophylline, the solution also contains CHOONa, Na_2SO_4, NaOH, NaCl, and various organic substances of unknown composition from the synthesis process. The synthesis process is composed of 10 steps with many accompanying reactions. When the solution was evaporated to dryness, the residue was about 10 wt% of the total mass of the solution (2). Therefore, the theophylline must be separated from the inorganic and the organic mixture for recovery.

Considering the large amount of theophylline in the solution, industrial-scale solvent extraction should be used for recovery. Unfortunately, data on the solvent extraction of theophylline has rarely been reported, except for the partition coefficient of theophylline in the heptane–water or chloroform–water systems as given by Takruri (3).

The objective of this work is to study the behavior of solvent extraction of theophylline and to develop a commercial process for the recovery of theophylline.

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EXPERIMENTAL

Materials

Theophylline was prepared by the Shandong Xinhua Pharmaceutical Company, Ltd., People's Republic of China. Its melting point was in the 270 to 274°C range.

The 2-ethylhexanol was industrial grade and met the specificity of the National Standard of the People's Republic of China, GB/T 6818-93 (4). Other solvents and chemicals used in this work were reagent grade and produced by the Beijing Chemicals Corp.

The original solution used in the pilot test was the mother solution after theophylline crystallization and was also prepared by the Shandong Xinhua Pharmaceutical Company, Ltd.

Apparatus

The RPC used for the pilot test was made of glass pipe with flanged connections. The bottom for settling the aqueous phase was 30 cm in height and 10 cm in diameter. The top section for segregating the organic phase was the same size as the bottom section but with an attached interface controller. The

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TABLE 1
The Parameters of RPC in the Pilot Test

Internal diameter of column	38 mm
Height of internals	5 m
Plate diameter	36 mm
Plate thickness	3 mm
Plate spacing	50 mm
Number of plates	98
Diameter of holes	10.8 mm
Arrangement of holes	Equilateral triangle
Triangular pitch	17 mm
Free area	0.366
Material	Stainless steel

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reciprocating plate stack was driven by a variable speed motor and an adjustable yoke. The RPC parameters are shown in Table 1.

A Davy-McKee 3-stage mixer-settler made of Plexiglass was used for stripping in the pilot test. There was a baffle plate on top of the mixer to improve liquid–liquid mixing. A 6-leaf closed pumping turbine with a sucker driven by an adjustable D.C. motor was used in each mixer. The settler interface was controlled by a hydrostatic leg. The mixer-settler parameters are given in Table 2.

Procedure

In the phase equilibrium experiment for extraction, the theophylline solution was fully mixed with solvent at different volume ratios. Then the theophylline concentration was determined by ultraviolet spectrophotometry. The maximum absorption is at 274 nm and pH 12–13, corresponding to the molar specific absorption coefficient, $\varepsilon_{\max}$, of 1.04–1.17. The absorbance is proportional to the concentration below 40 mg/L theophylline concentration. A 752C spectrophotometer was used in this work. In determining the theophylline con-

TABLE 2
The Parameters of Mixer-Settler in the Pilot Test

Size of mixer	10 × 10 × 10 cm
Size of settler	10 × 20 × 14.5 cm
Number of stages	3
Impeller	Closed 6-leaf turbine with sucker
Turbine diameter	39 mm
Size of leaf	12 × 8 mm

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centration of the solution, other organic impurities will interfere with the process. To separate the impurities, the theophylline in the original solution was extracted using 2-ethylhexanol in a multiple stage process. The absorbance of the raffinate was subtracted as background from that of the solution. In the pilot test the throughput of the original solution and the 2-ethylhexanol through the column was determined by filling the column with the aqueous phase and then feeding the organic phase into the inlet located at the bottom of the plate stack. After the flow ratio of the organic phase to the aqueous phase, O/A, was fixed at a given amplitude and frequency of pulsation, the flow rates of the two phases were increased gradually until flooding occurred. The mass transfer was determined by measuring the concentration–time relationships of the two phases at the outlets from startup to steady state. The extraction efficiency was calculated from the inlet and the outlet theophylline concentration of the aqueous effluent at steady state. In the stripping test the loaded 2-ethylhexanol as the continuous phase in the mixer was first filled. To accelerate equilibrium, each settler was first filled with half aqueous phase and half organic phase.

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RESULTS AND DISCUSSION

Selection of Solvent for Extraction

For industrial applications the following factors should be considered in the selection of an extraction solvent for theophylline: 1) suitable distribution between phases and capacity for extraction of theophylline; 2) low solubility in the effluent and high boiling point to decrease loss in solution and loss due to volatilization; 3) easily stripped or regenerated; 4) good physical properties for mass transfer such as viscosity, density, and interfacial tension with water; and 5) safe, nontoxic, and low cost.

In experiments for the selection of a solvent, the theophylline distribution ratio between the solvent and the saturated solution of theophylline in deionized water was determined at ambient temperature and pH 6–7. Tributyl phosphate has a high distribution ratio but is very expensive for commercial use. 1-Butanol also has a high distribution ratio but dissolves in water to 7.8 wt% at 20°C, which would necessitate a recovery system for 1-butanol. The data in Table 3 shows that 2-octanol or 2-ethylhexanol both have reasonable distribution ratios and low solubilities; 0.05 wt% at 20°C for 2-octanol and 0.06 wt% at 25°C for 2-ethylhexanol. Therefore, either solvent could be used for recovery of theophylline. Because 2-ethylhexanol is in stable supply at a lower price in China, it was selected as the solvent for recovery of theophylline although it does have some drawbacks, for example, slightly higher viscosity and some organic impurities will dissolve in it.

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TABLE 3
Distribution Ratio of Theophylline Extracted by Several Solvents, O/A = I. Ambient Temperature

Tributyl phosphate	2.3
Di-(2-ethylhexyl) phosphoric acid	0.3
Methyl isbutyl ketone	0.2
n-Butyl alcohol	1.74
n-Butyl alcohol:octanol-1 = 1:1 v / v	1.02
Trioctylamine:kerosene = 1:1 v / v	0.26
2-Ethylhexanol	0.81
2-Octanol	0.7

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Theophylline Distribution Behavior

Theophylline–2-Ethylhexanol–Water System

The distribution ratio was measured at equilibrium for a theophylline solution of 2.15 g/L at pH 7 with 2-ethylhexanol at O/A = 0.5–10.0 v/v. The theophylline concentration in the organic phase is plotted against that in the aqueous phase in Fig. 1. The mean distribution ratio was determined from the slope of the linear relation to be 0.81.

The distribution ratio was also determined experimentally in the 10 to 60°C range at pH 5 and O/A = 1 v/v for 2.98 g/L of the original theophylline concentration. The result, Fig. 2, shows that the distribution ratio improves with increasing temperature. In addition, the phase segregation is also accelerated with increasing temperature because the viscosity decreases with increasing temperature.

The extraction distribution ratio is also very dependent on the pH of the solution, Fig. 3(A). The maximum distribution ratio is below pH 6, while for pH greater than 8 the distribution ratio drops drastically to near zero. This behavior allows the pH to be used as a controlling factor for stripping loaded 2-ethylhexanol in the recovery process.

Theophylline can be considered to be a very weak acid since the proton on the nitrogen in position 7 of the heterocyclic ring is dissociable. The dissociation constant pK_a is 8.6 as determined by potentiometry and spectrophotometry (5). The ratio of undissociated theophylline molecules to the total theophylline concentration in the pH range can be calculated using the dissociation constant, Fig. 3(B). The data show that theophylline can only be extracted by 2-ethylhexanol in molecular form because the relationship between the undissociated ratio of theophylline to the pH is very similar to that of the distribution ratio of theophylline to the pH.

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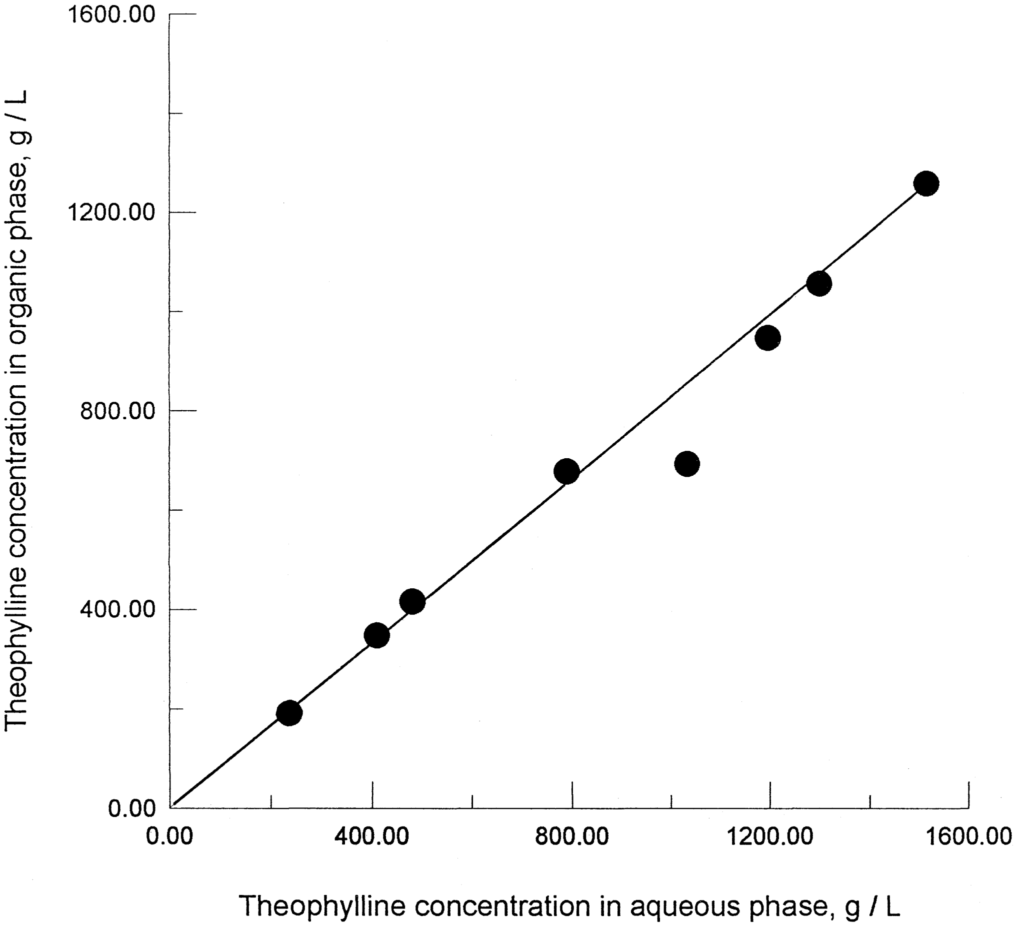

FIG. 1 Distribution of theophylline in 2-ethylhexanol–water system.

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Original Solution–2-Ethylhexanol System

The pH of the original solution is 12–13 and the theophylline in the basic solution exists in the form of 1,3-dimethylxanthine sodium salt ($C_7H_7N_4NaO_2$). The pH was adjusted to 7 using H_2SO_4 and then the theophylline in the original solution was extracted by 2-ethylhexanol at different O/A values. The equilibrium concentrations of each phase are show in Fig. 4. The distribution ratio is 0.7 as obtained from the slope of the straight line at 15°C.

The effect of Na_2SO_4 concentration in the original solution on extraction was also studied experimentally by adding different amounts of Na_2SO_4 to the original solution. The distribution ratio increased with increasing Na_2SO_4 concentration, Fig. 5. This salting-out effect is similar to the caffeine extraction process (6).

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Stripping of Loaded 2-Ethylhexanol

The theophylline in the loaded 2-ethylhexanol is transferred into the aqueous phase at $pH > 8$ by the reaction

$$C_7H_8N_4O_{2(org)} + NaOH_{(aq)} = C_7H_7N_4O_2Na_{(aq)} + H_2O$$

The effects of the amount of NaOH and the contact time between the organic phase and the aqueous phase on stripping were then studied experimentally.

2-Ethylhexanol–Theophylline–NaOH Solution System

The theophylline solution in 2-ethylhexanol was prepared by adding theophylline to 2-ethylhexanol to the desired concentration. The solution was then stripped with NaOH solution in deionized water. As mentioned above, the distribution ratio is near zero since the pH of the NaOH solution is higher than 8.

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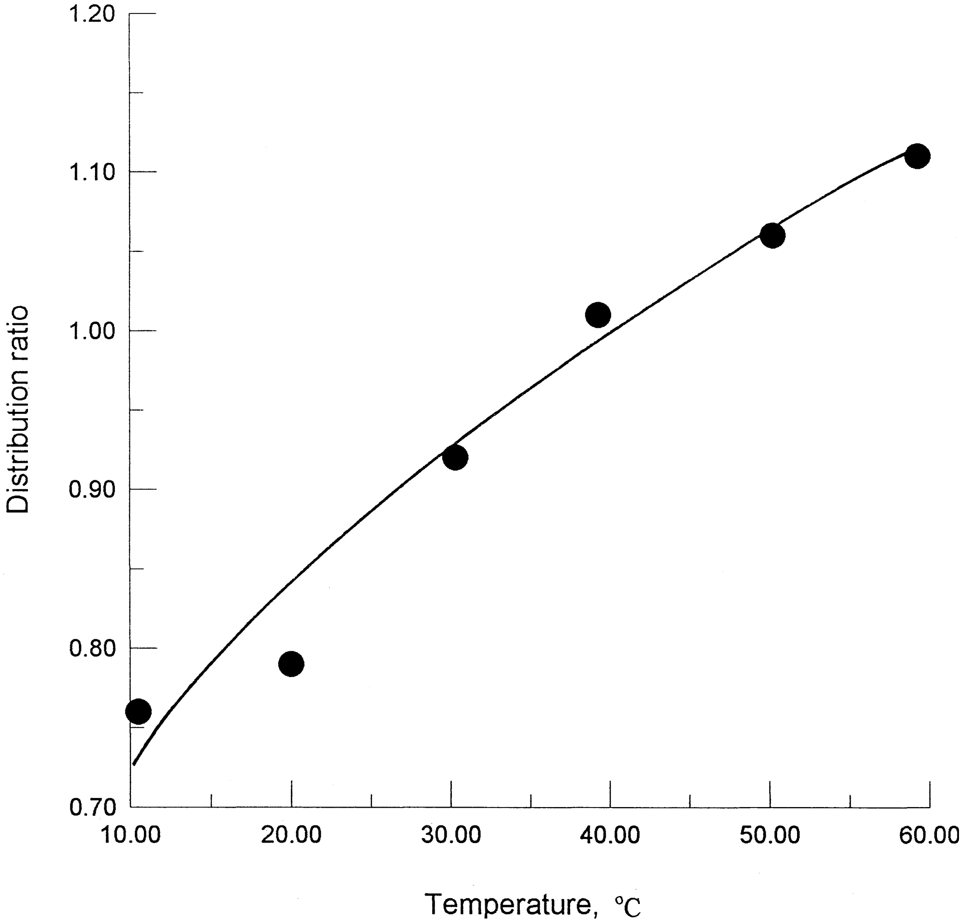

FIG. 2 Effect of temperature on distribution ratio of theophylline in 2-ethylhexanol–water system.

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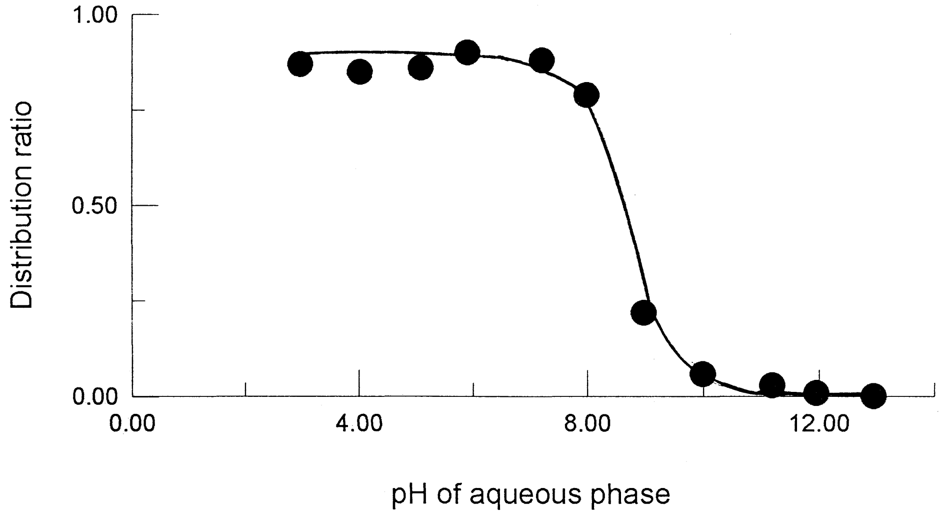
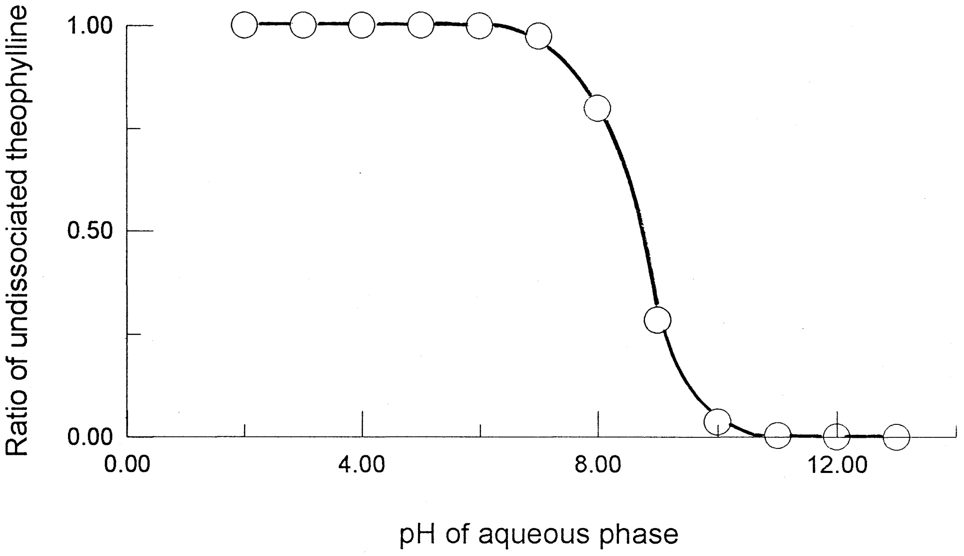


(A) Effect of pH on distribution ratio of theophylline determined experimentally



(B) Ratio of undissociated theophylline molecule to total theophylline concentration

FIG. 3 Effect of pH on distribution ratio of theophylline.

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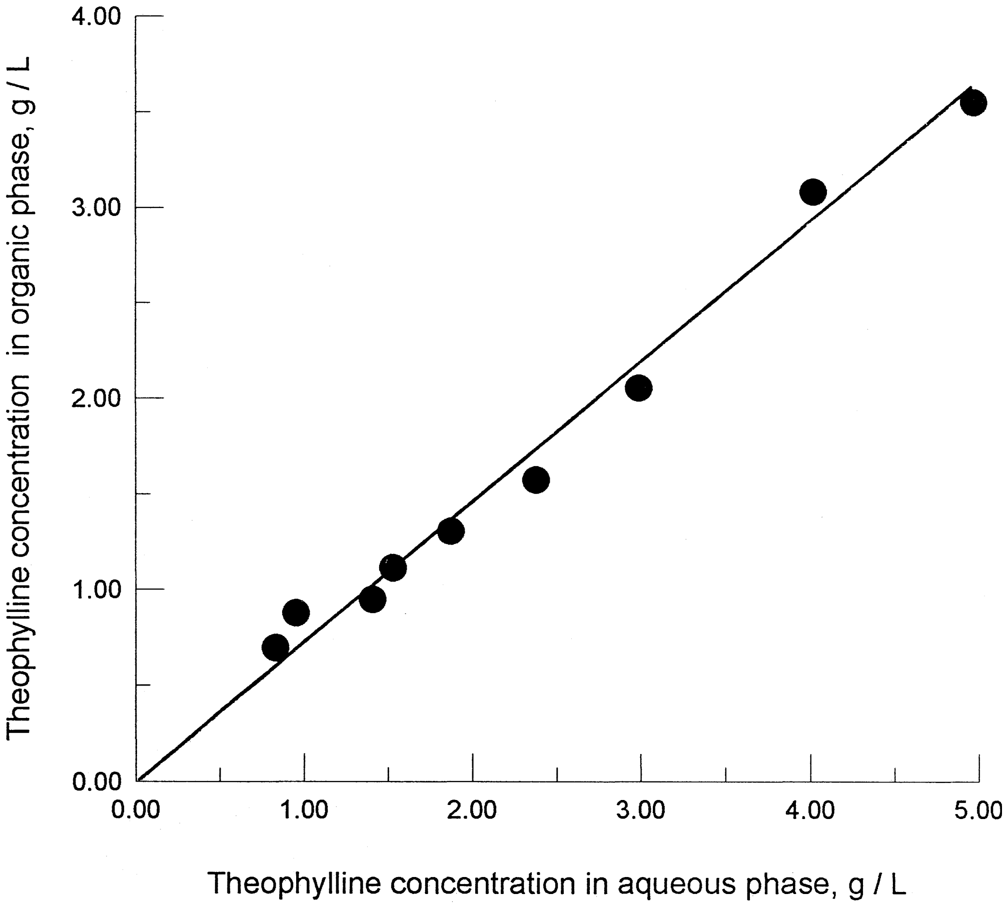

FIG. 4 Distribution of theophylline in 2-ethylhexanol–mother solution system.

It was expected that the theophylline would be totally stripped by pH $>$ 8 NaOH solution in a one-stage contact, but the experimental results showed that the stripping was not complete. The distribution of theophylline in the 2-ethylhexanol–NaOH solution system is shown in Table 4.

The data shows that the stripping efficiency only depends on the molar ratio of NaOH to theophylline and that the NaOH concentration and the phase ratio normally have no effect on the stripping. If the molar ratio is less than 1, total stripping is impossible regardless of the conditions. To complete the stripping, the amount of NaOH should be greater than the stoichiometric value; for example, the molar ratio should be great than 1.5.

2-Ethylhexanol in Equilibrium with the Original Solution–NaOH Solution System

The 2-ethylhexanol in equilibrium with the original solution is different from the 2-ethylhexanol solution of theophylline in that some organic impuri-

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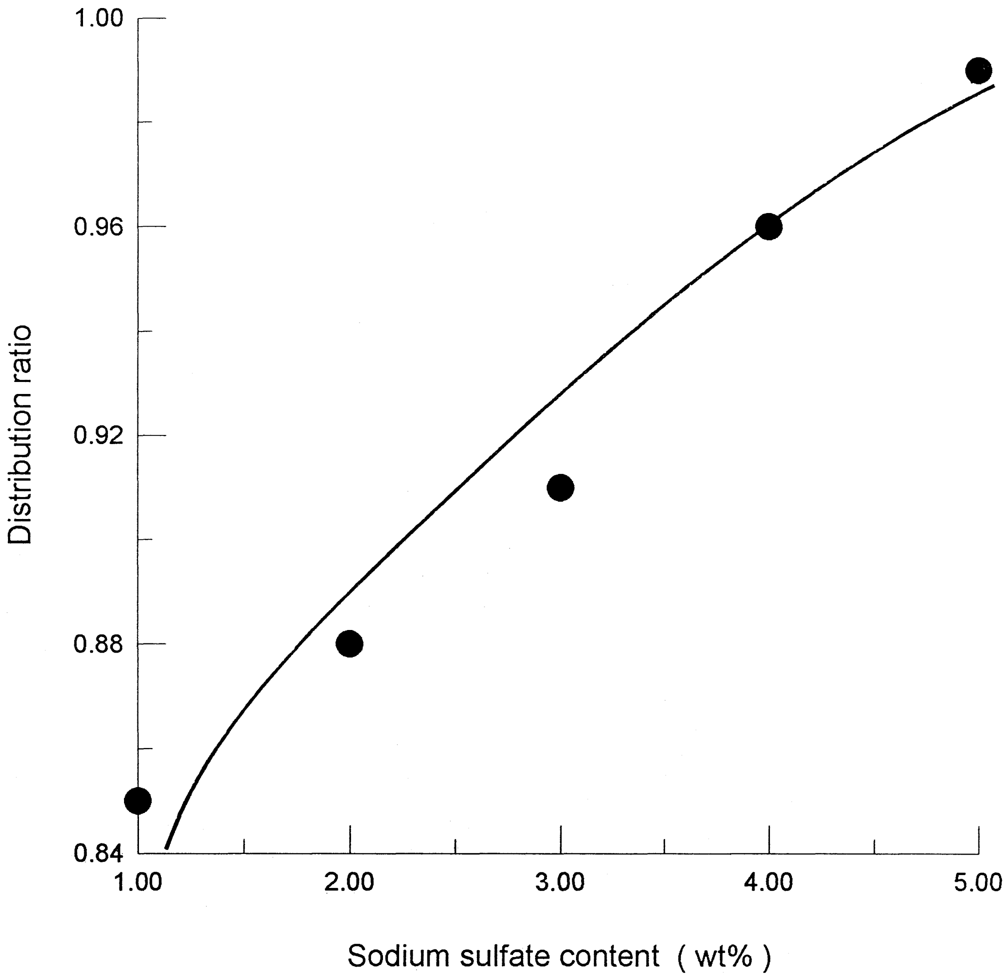

FIG. 5 Effect of sodium sulfate content on distribution ratio.

TABLE 4

Distribution of Theophylline in 2-Ethylhexanol-NaOH Solution System

Original NaOH concentration (mol/L)	Original theophylline concentration (g/L)	O/A	Aqueous concentration in equilibrium (g/L)	Organic concentration in equilibrium (g/L)	Molar ratio NaOH: Theophylline	Stripping efficiency
0.001	1.085	5.0	1.081	0.869	0.033	0.199
0.001	1.085	2.5	0.908	0.722	0.066	0.334
0.001	1.085	1.7	0.807	0.601	0.099	0.446
0.001	1.085	1.3	0.704	0.522	0.132	0.518
0.01	1.085	5.0	3.180	0.449	0.338	0.586
0.01	1.085	2.5	2.580	0.054	0.677	0.950
0.01	1.085	1.7	1.803	0.003	1.020	0.997

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ties are also extracted into the organic phase. To further enrich the theophylline, a large phase ratio, O/A = 20, was used for the stripping with an original theophylline concentration in the 2-ethylhexanol at 1.706 g/L. The theophylline concentration in the 2-ethylhexanol at different stirring times was determined as shown in Fig. 6. The results show that the contact time is another important factor for stripping, and that mass transfer may play a considerable role in stripping.

Recovery Process Design

The recovery process design is based on the parameters listed in Table 5.

The recovery process has three unit operations: 1) Adjust the pH of the original solution from 13 to 6–7 to transform the solute from 1,3-dimethylxanthine sodium salt to theophylline. 2) Extract the theophylline from the solution with 2-ethylhexanol to separate it from the inorganic impurities and

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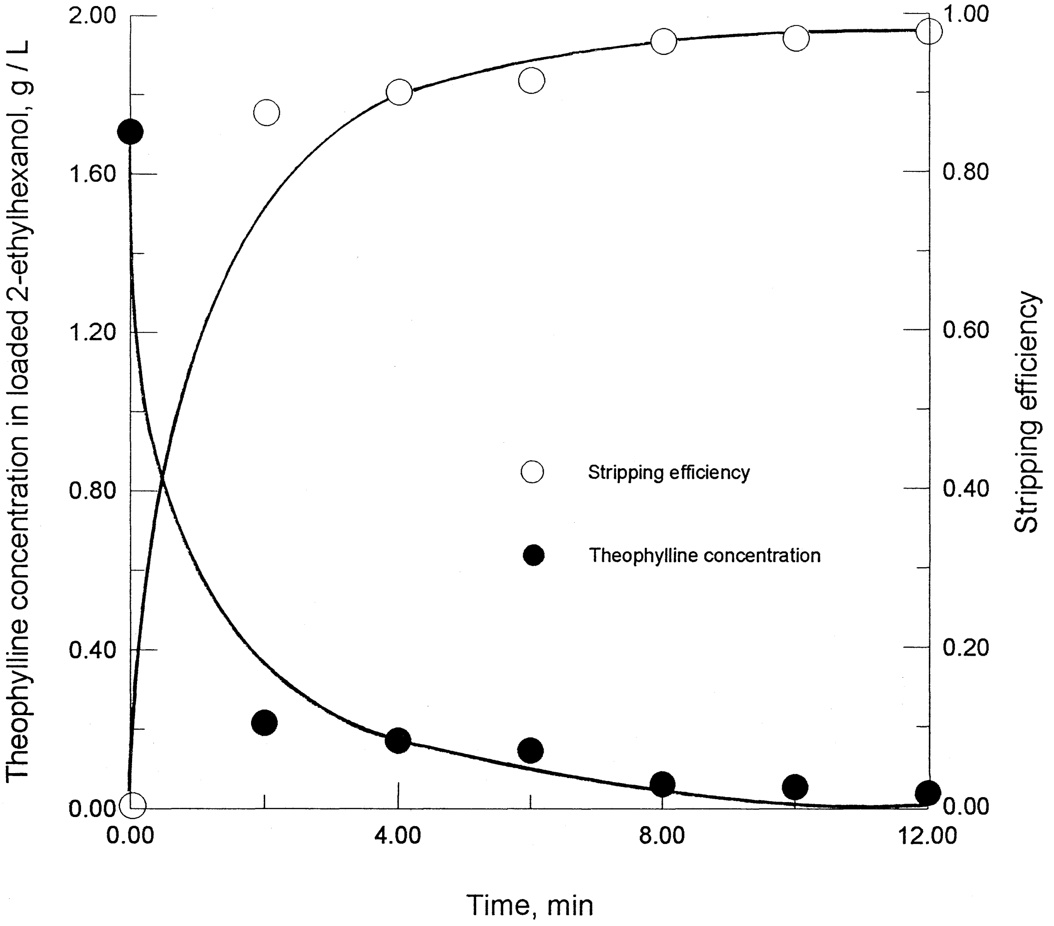

FIG. 6 Effect of stirring time on stripping efficiency.

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TABLE 5
Specificity of Recovery Process

Throughput of the mother solution	3.4 t/h
Recovery of extraction theophylline	>0.90
Original content of theophylline in the mother solution	0.6 wt%
Solvent content in raffinate	$<0.05\%$

most of the organic impurities by 4-stage countercurrent extraction with a flow ratio of 2, then remove the residual 2-ethylhexanol in the raffinate using a polypropylene fiber bed, finally the raffinate is pumped to a waste treatment system; 3) Strip the 2-ethylhexanol with 0.2–0.4 mol/L NaOH solution at a flow ratio of 10. Recycle the discharged 2-ethylhexanol for extraction. The stripping solution is used to produce caffeine. The recovery process is shown in Fig. 7.

Pilot Test

Extraction by 2-Ethylhexanol in RPC

To evaluate the capacity of RPC for the 2-ethylhexanol–original solution system, the flooding velocity was determined experimentally in the pilot test column shown in Table 1. The flooding velocity, $V_c + V_d$, is the sum of the superficial velocity of the continuous phase, V_c, and that of the dispersed phase, V_d. In the experimental system the flow ratio varied from 1 to 3 and the pulse frequency from 1.6 to 2.7 Hz with a pulsation amplitude of 13 mm. The

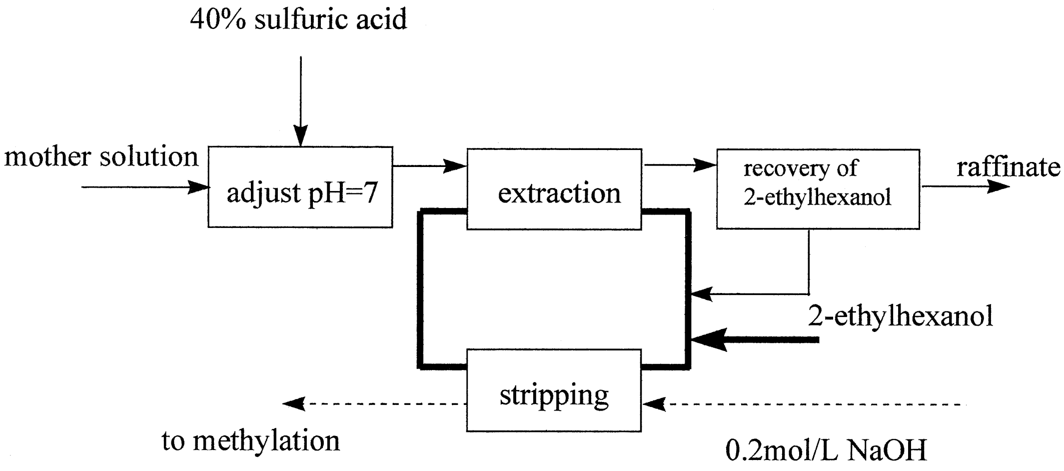

FIG. 7 Recovery process of theophylline.

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relationship between the flooding velocity and the pulsation intensity, Fig. 8, shows that the RPC is flexible in operation in this flow ratio range for extraction from the original solution. The mass transfer test was also performed in the RPC pilot test column with the original solution and 2-ethylhexanol. The flow ratio was set at 2, the pulsation frequency at 2 Hz, and the amplitude at 13 mm. The results, Table 6, show that the HETS for the original solution–2-ethylhexanol system is 0.869–0.877 m.

The startup process was also investigated experimentally. As mentioned in the test procedure, the column was first filled with the aqueous phase before pulsing. The variation of theophylline concentration in each phase was then determined over time, Fig. 9. The results show that the startup process in the pilot column required about 180 minutes to reach stable operation for the given operating conditions.

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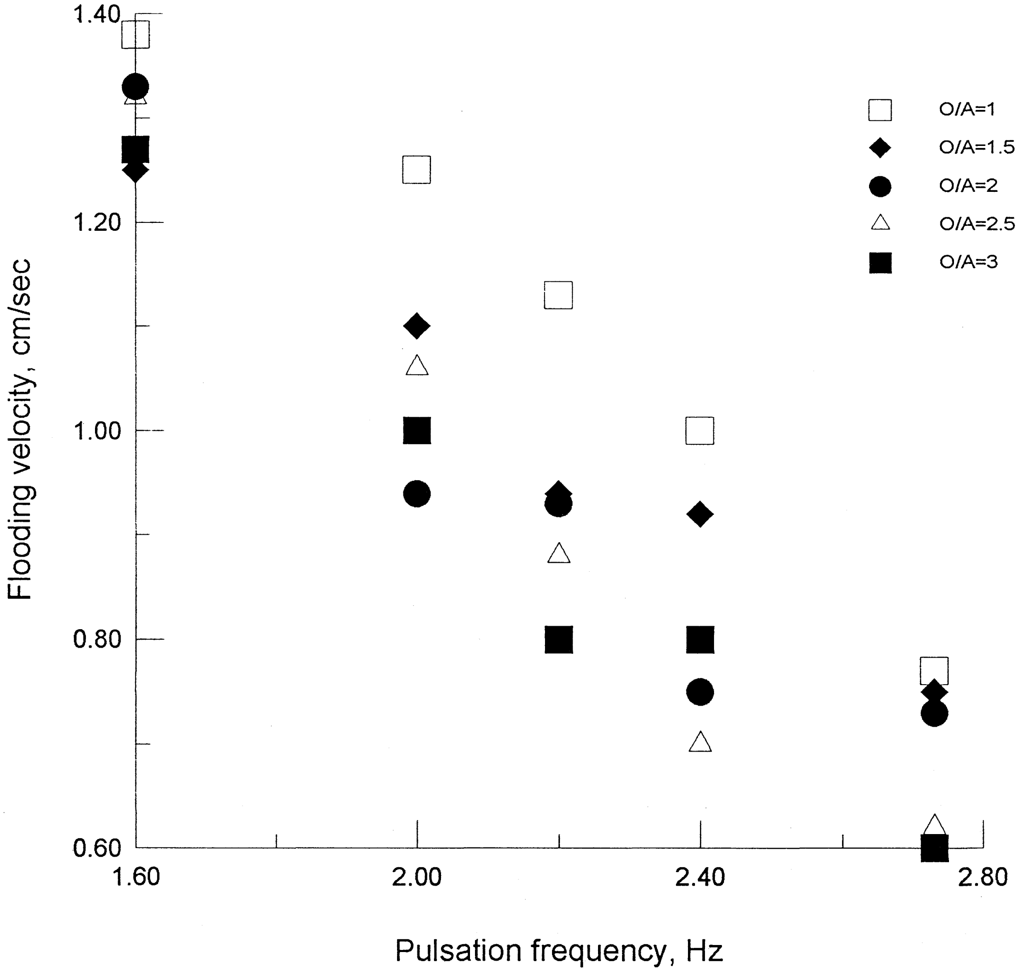

FIG. 8 Flooding velocity of RPC.

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TABLE 6
RPC Mass Transfer of Theophylline Extraction in the Pilot Test. Pulsation Stroke = 13 mm, Frequency = 120/min, Flow Ratio O/A = 2, Ambient Temperature

pH of the mother solution	Original concentration in aqueous phase (g/L)	Original concentration in organic phase (g/L)	Aqueous concentration in equilibrium (g/L)	Organic concentration in equilibrium (g/L)	Recovery	HETS (m)
5.70	6.008	0	0.280	2.486	0.953	0.877
5.70	5.671	0	0.289	2.112	0.954	0.869
6.26	5.446	0.124	0.248	1.633	0.954	0.869

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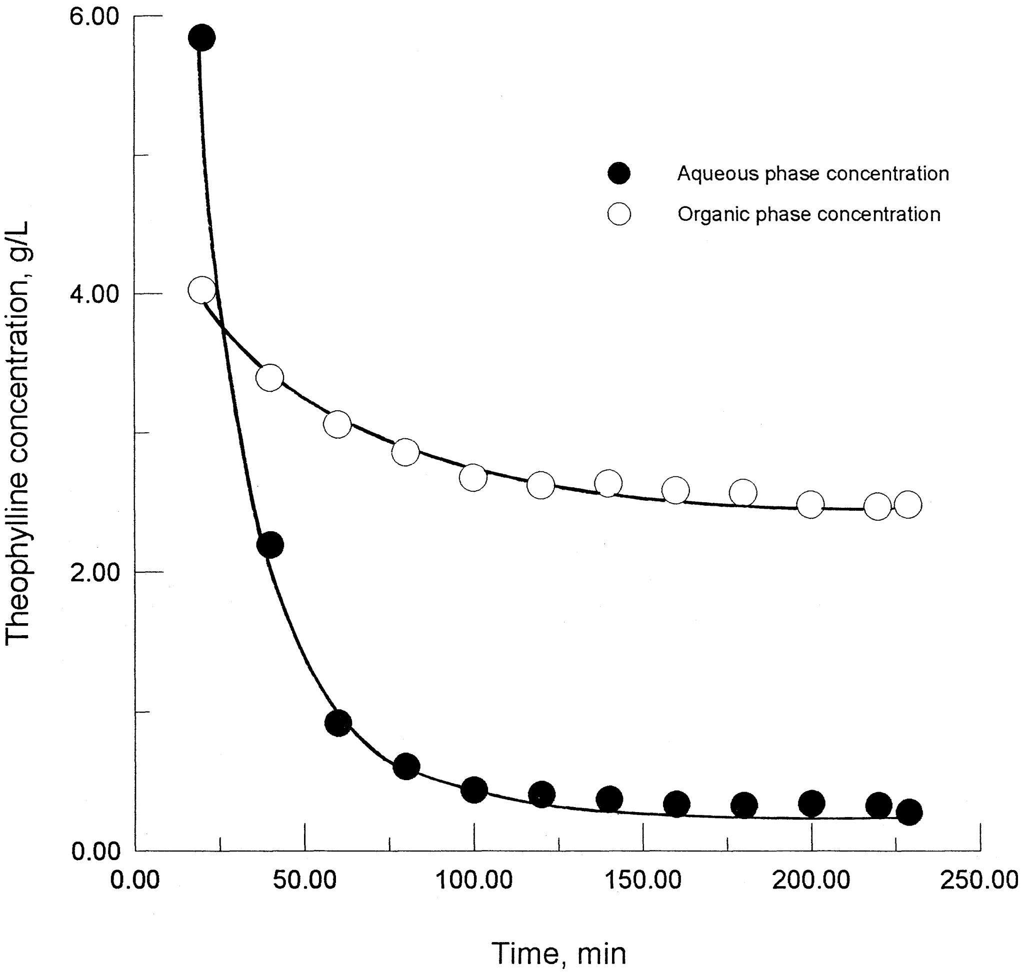

FIG. 9 RPC starting process.

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Stripping in the Mixer-Settler

For the stripping pilot test the NaOH concentration was varied from 0.2 to 0.6 mol/L, the organic to aqueous phase flow ratio was set to 10, and the mixer stirring speed was set in the 800 to 1000 rpm range. The results for 3-stage countercurrent stripping are given in Table 7.

The results show that the mixer-settler residence time was sufficiently long for efficient stripping and that the residual concentration of theophylline in the discharged 2-ethylhexanol was lower than 30 mg/L. The discharged 2-ethylhexanol was then recycled to the extraction unit. Any change in the theophylline distribution ratio between the 2-ethylhexanol and the original solution was not found after 63 cycles. The phase segregation in the settler was effective at ambient temperature. At slightly higher temperatures, 30°C for example, the segregration was not improved further but the stripping efficiency was remarkably decreased.

Scaleup Design and Commercial Application

The Karr correlation for scaleup design of RPC has been demonstrated by many examples (7, 8). A pair of 500 mm diameter RPCs were used to treat 3.4 t/h of the original solution. For the 500-mm diameter column, the plate spacing, the total throughput per unit area of the column section, and the amplitude were kept the same as for the pilot column. Instead of one large diameter column, the two columns were used side by side to allow operating flexibility. A small heat exchanger in the inlet of the aqueous phase was used to heat the feed in winter. The internal parameters for the 500-mm diameter column are given in Table 8.

TABLE 7
Stripping by Mixer-Settler in the Pilot Test. Flow Ratio O/A = 10. Stripping Efficiency = (Original Concentration of Organic Phase − Outlet Concentration of Organic Phase)/Original Concentration of Organic Phase

Original concentration of organic phase (g/L)	Origina concentration of NaOH (g/L)	Molar ratio NaOH/ theophylline	Stirring speed (rpm)	Temperature (°C)	Stripping efficiency
2.927	0.6	3.69	800	24	0.991
2.164	0.4	3.33	810	23	0.989
1.498	0.2	2.40	1000	18	0.986
2.309	0.4	3.12	900	40	0.977

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TABLE 8
Geometry of 500 mm Diameter Column

Height of internals	11.55 m
Allowance between plate and tower wall	4.5 m
Plate thickness	2.5 mm
Plate spacing	50.0 mm
Number of plates	220
Diameter of holes	10.8 mm
Triangular pitch	17.0 mm
Free area	0.366
Material	Stainless steel

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The scaleup design of the Davy-McKee mixer-settler was based on having the same residence time and the same specific input power as the pilot mixer-settler (9). A adjustable speed motor was used to drive the impeller turbine in each stage for more flexible operation. Each settler had an independent weir to control the interface of each stage. The details of the scaledup mixer-settler are given in Table 9.

The commercial scale theophylline recovery system using 2-ethylhexanol extraction has been operated successfully for 2 years and has met all the expected design characteristics. The theophylline extraction efficiency is 0.987 for the first 500 mm diameter column and 0.973 for the second column. The extraction efficiency is higher than the 0.952 obtained in the pilot test. A pulsation frequency of 2 Hz is used, which is slightly higher than that calculated by the Karr correlation. No doughnut-type baffles were inserted in the stack of the 500 mm-diameter column, showing that baffles are not necessary in a 500-mm diameter column. Some unexpected suspended particles appeared in the original solution during operation, but no flooding or plugging occurred in the columns. The Karr column is quite suitable for treatment of the feed with suspended particles.

TABLE 9
Parameters of Davy-McKee Mixer-Settler for Scaleup Design

Size of mixer	1.2 × 1.2 × 1.1 m
Size of settler	2.2 × 1.2 × 1.5 m
Number of stages	3
Impeller	Closed 6-leaf turbine with sucker
Turbine diameter	320 mm
Size of leaf	120 × 111 × 4 mm

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The 500-mm diameter column is hydrodynamically stable for long period operation with a total superficial velocity of 0.007 m/s and a hold-up of about 0.15. The result is similar to that of the pilot test column. When the Karr correlation is used for design of a full size column, the hydrodynamic effect will be negligible. For mass transfer, the HETS of the 500-mm diameter column is 1.25–1.60 m, indicating that the exponent in the Karr correlation should be 0.187, which is very close to the 0.19–0.36 range for the MIBK–acetic acid–water system given by Lo (10). For a safer design, an exponent of 0.38 could be used in the Karr correlation.

The Davy-McKee mixer-settler has also been used successfully. The stirring speed is 300 rpm and the flow ratio of the loaded organic phase to the aqueous phase is 10. The residual theophylline concentration in the outlet of the mixer-settler is about 320 mg/L, which is higher than that of the pilot test, but has had no effect on recycling and extraction for the theophylline recovery system. The polypropylene fiber bed effectively removes the entrained 2-ethylhexanol in the raffinate from the extraction column. The 2-ethylhexanol concentration in the raffinate was about 130 mg/L. This loss is an acceptable operating cost.

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CONCLUSIONS

(1) 2-Ethylhexanol can be used as a commercial extraction solvent for recovery of theophylline in the mother solution after crystallization in the synthesis process. The theophylline distribution is mainly governed by the pH of the original solution. The distribution ratio is 0.81 at pH 7 and near zero for pH > 8. Therefore, the loaded 2-ethylhexanol can be stripped by NaOH solution. The extraction distribution ratio is also improved by higher temperature and higher Na_2SO_4 concentration. Over 95% of the theophylline in the original solution can be recovered by 4-stage countercurrent extraction with a O/A $= 2$ flow ratio.

(2) RPC is a suitable commercial extractor with good flexibility and stability for the recovery process. Because of the higher free area and large hole diameter in the sieve plate, RPC is also suitable for treatment of feed having suspended particles. A 500-mm diameter column was designed successfully using the Karr correlation, which shows that the Karr correlation is very appropriate for engineering application even though the scaleup may be slightly conservative.

REFERENCES

1. Z. Sigui, *Technology Handbook of Fine Organic Chemicals*, Science Press, Beijing, 1991, p. 387 (in Chinese).
2. H. Xien, B. Runsheng, W. Xuejun, et al., *J. Tsinghua Univ*. (*Sci. Technol.*), *36*(12), 13 (1996).

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3. H. Takruri, B. Ecanow, and R. Balagot, *J. Pharm. Sci.*, *66*, 283 (1977).
4. The National Standard of the People's Republic of China, GB/T 6818-93, *2-Ethylhexanol for Industrial Use* (1994).
5. H. V. Maulding and M. A. Zoglio, *J. Pharm. Sci.*, *60*, 309 (1971).
6. H. Xien, D. Weizhi, W. Xuejun, et al. *J. Tsinghua Univ.* (*Sci. Technol.*), *35*(3), 13 (1995).
7. T. C. Lo, M. H. I. Baird, and R. N. V. Rama, *Chem. Eng. Commun.*, *116*, 67 (1992).
8. X. Hu, *Sep. Sci. Technol.*, *32*(12), 2039 (1997).
9. G. C. I. Warwick and J. B. Scuffham, in *Handbook of Solvent Extraction* (T. C. Lo, M. H. I. Baird and C. Hanson, Eds.), Wiley, New York, NY, 1983, p. 287.
10. T. C. Lo, in *Handbook of Separation Techniques for Chemical Engineers*, 2nd ed. (P. A. Schweitzer, editor-in-chief), McGraw-Hill, New York, NY, 1988, p. 1-343.

Received by editor September 25, 1998
Revision received January 1999

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