Solubilities of *o*-, *m*- and *p*-Coumaric Acid Isomers in Carbon Dioxide at 308.15−323.15 K and 8.5−25 MPa

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The solubilities of isomeric *o*-, *m*- and *p*-coumaric acids in high-pressure carbon dioxide were measured using a flow-type experimental apparatus at (308.15, 313.15, and 323.15) K and (8.5, 10, 15, 20, and 25) MPa, respectively. The data were modeled by a density model-based correlation. We found that *m*-coumaric acid showed the highest solubility and *o*-coumaric acid showed the lowest solubility at the experimental supercritical conditions.

Introduction

In general, an extract obtained by supercritical fluid extraction from natural products contains various bioactive substances and their derivatives as well as isomers. For example, in the isolation of coumaric acids for pharmaceutical purposes from a target natural plant (e.g., *Morus alba*), there exist several isomers (*o*-, *m*-, and *p*-coumaric acid) and coumarin derivatives in the extract (Noh et al., 1977). Thus, to obtain high-purity coumaric acid, it is of importance to know the variation of solubility among the isomeric coumaric acids in a supercritical fluid. However, there appears to be no literature data on the solubility of coumaric acids in supercritical CO_2.

In the present study, the solubility of *o*-, *m*-, and *p*-coumaric acids in supercritical carbon dioxide were measured over a wide range of pressure at three isotherms. An attempt was made to correlate the measured data using a semiempirical density model (Bartle et al., 1991; Özcan et al., 1997).

Experimental Section

Reagents and Experiment. High-purity coumaric acids were purchased from Sigma Chemical Co., United States. The purity of *o*-coumaric acid was 98%, *m*-coumaric acid was 98%, and *p*-coumaric acid was 98%. CO_2 (99.9%) was purchased from the Seoul Gas Co. (Seoul, Korea). A schematic diagram of the flow-type microscale phase equilibrium apparatus is shown in Figure 1. It is described in detail elsewhere (Yoo and Hong, 1996; Choi et al., 1996). The internal volume of the equilibrium cell was 60 cm^3. A syringe pump (ISCO 260DM, United States) with an accuracy 2% range of full scale was used for feeding carbon dioxide. Pressure was controlled within ±5 Pa by a back-pressure regulator (TESCOM 26−1700, United States) and the pressure was measured by a Heise gauge (HEISE, MM-43776, United States) within an uncertainty range of ±0.05 MPa. The equilibrium cell was immersed in an air bath, and the temperature was controlled by a PID controller. The error range of measured temperatures was within ±0.1 K, which was checked by a standard high-precision thermometer (Witeg, Germany). Liquid CO_2 at ambient temperature is charged to the system and compressed to the desired operating pressure. After the saturated CO_2-rich phase exists, the equilibrated effluent was passed through methanol-filled two-step cold traps and a heated metering valve. Measurements were made at (308.15, 313.15, and 323.15) K and pressures oft (8.5, 10, 15, 20, and 25) MPa. The experiment was repeated more than three times for each sample solute.

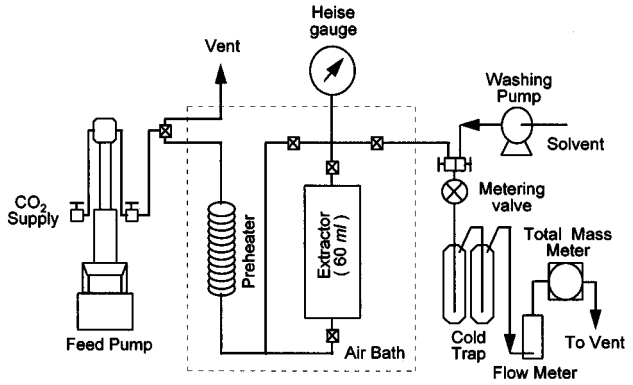

Figure 1. Schematic diagram of the flow-type equilibrium cell.

Table 1. Calibrated Results of HPLC for *o*-, *m*-, and *p*-Coumaric Acids

	concentration [mg/mL] = b_1 × HPLC area + b_0		
solute	$10^9\ b_1$	$10^4\ b_0$	γ^2
o-coumaric acid	9.149	0.661	0.999
m-coumaric acid	6.314	1.409	0.996
p-coumaric acid	6.282	11.639	0.997

HPLC Analysis. The separated solutes were dissolved by methanol in the cold trap. This dissolved solute was expanded and diluted further with additional methanol and analyzed by HPLC (Milton Roy, United States). The column was YMC pack, ODS-A (250 × 4.6 mm) with detection by 280 nm UV (Casteele et al., 1983). The calibration results for coumaric acids are shown in Table 1.

Correlation of Solubility Data

Although the quantitative calculation of solubility of bioactive substances in supercritical fluids is difficult and frequently erroneous, a simple semiempirical method (Bartle et al., 1991; Özcan et al., 1997) was used for the correlation of the experimental data. The following equa-

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Table 2. Parameters Used in the Calculation of Solubility from Eq 1

solute	A	b/K^{-1}	10^2c/kg m^{-3}	AAD%[a]
o-coumaric acid	26.55	−12 011.5	1.21	26.5
m-coumaric acid	24.14	−10 894.7	1.08	37.5
p-coumaric acid	23.88	−11 147.9	1.18	27.8

[a] AAD% = $[\sum_{i=1}^{N}|\{\langle y_{2,i}\rangle - y_{2,i}^{cal}\}/\langle y_{2,i}\rangle| \times 100]$, where the superscript 'cal' denotes calculated mole fraction solubility.

Table 3. Measured Average Mole Fraction, $\langle y_2\rangle$, of Coumaric Acid Isomers in CO_2

		$10^8\langle y_2\rangle$ [RSD%[a]]		
T/K	p/MPa	*o*-coumaric acid	*m*-coumaric acid	*p*-coumaric acid
308.15	8.5	1.10 [10.4]	3.11 [17.6]	1.50 [18.6]
	10.0	3.81 [8.9]	13.89 [17.9]	5.63 [5.8]
	15.0	8.10 [9.6]	32.52 [3.6]	11.67 [3.2]
	20.0	14.36 [5.1]	38.38 [0.5]	15.70 [3.8]
	25.0	17.54 [8.5]	52.63 [0.2]	17.58 [3.9]
313.15	8.5	0.82 [19.5]	2.14 [23.3]	0.79 [17.7]
	10.0	2.62 [16.4]	10.30 [0.9]	2.65 [18.4]
	15.0	9.35 [0.8]	32.59 [0.8]	14.70 [6.2]
	20.0	19.85 [0.5]	58.59 [2.9]	20.86 [10.1]
	25.0	25.99 [8.4]	70.11 [3.4]	26.98 [10.3]
323.15	8.5	0.21 [14.2]	0.16 [6.2]	0.52 [11.7]
	10.0	1.16 [1.7]	4.27 [1.8]	0.63 [7.9]
	15.0	14.01 [5.2]	38.11 [11.2]	16.25 [3.3]
	20.0	25.04 [9.5]	63.81 [9.2]	27.54 [5.4]
	25.0	35.38 [9.6]	105.55 [6.6]	38.54 [5.6]

[a] RSD%: percent of relative standard deviation. RSD% = SD/$\langle y_2\rangle \times 100$, where SD = $[(1/N)\sum_{i=1}^{N}(y_{2,i} - \langle y_2\rangle)^2]^{0.5}$ and $\langle y_2\rangle$ denotes average mole fraction.

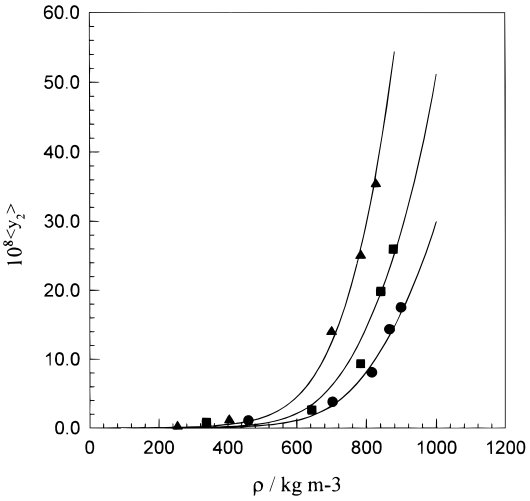

Figure 2. Average solubility in mole fraction, $\langle y_2\rangle$, for *o*-coumaric acid in supercritical CO_2. The graph shows the comparison of calculated curves and experimental points plotted versus density,ρ, of the solubility: (●) 308.15 K; (□) 313.15 K; (▲) 323.15 K.

tion was used

$$\ln\left(\frac{y_2 p}{p_{ref}}\right) = a + \frac{b}{T} + c(\rho - \rho_{ref}) \qquad (1)$$

where y_2 is the mole fraction solubility, p is the pressure, a, b, and c are constants, p_{ref} is a standard pressure of 1 bar, ρ is the density of the solution, and ρ_{ref} is a reference density for which a value of 700 kg m^{-3} was used. T is the absolute temperature. The values of the a, b, and c parameters given in Table 2 were the average for each coumaric acid isomer. The fitting errors (AAD %) for each solute are also shown in Table 2.

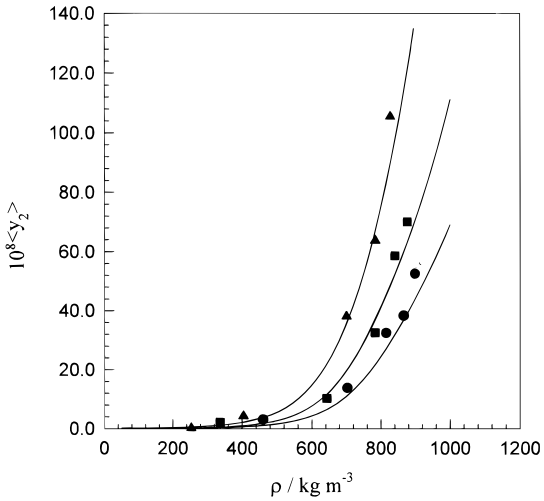

Figure 3. Average solubility in mole fraction, $\langle y_2\rangle$, for *m*-coumaric acid in supercritical CO_2. The graph shows the comparison of calculated curves and experimental points plotted versus density,ρ, of the solubility: (●) 308.15 K; (■) 313.15 K; (▲)323.15 K.

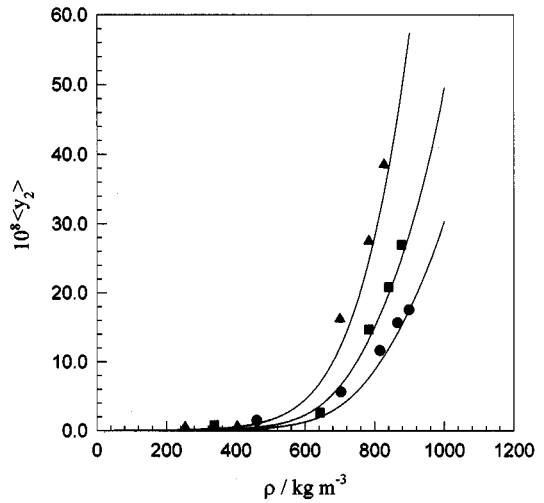

Figure 4. Average solubility in mole fraction, $\langle y_2\rangle$, for *p*-coumaric acid in supercritical CO_2. The graph shows the comparison of calculated curves and experimental points plotted versus density, ρ, of the solubility: (●) 308.15 K; (■) 313.15 K; (▲) 323.15 K.

Results and Discussion

Experiments were repeated three to five times for each condition. Data were reported here as the averaged mole fraction solubility, $\langle y_2\rangle$ of *o*-, *m*- and *p*-coumaric acids in CO_2 at (308.15, 313.15 and 323.15) K and (8.5, 10, 15, 20, and 25) MPa, respectively. They are summarized in Table 3 with the percent relative deviation (RSD %). *m*-Coumaric acid showed the highest solubility in CO_2, while *o*- and *p*-coumaric acids showed similar low solubility. For each coumaric acid, solubility tends to increase with increasing temperature and pressure.

Finally, the calculated solubilities using eq 1 were compared with the experimental values for *o*-, *m*-, and *p*-coumaric acids in Figures 2, 3 and 4, respectively. Agreement between the calculated and experimental values for *o*-, *m*-, and *p*-coumaric acids is good. Therefore, solubility can be confidently calculated at any temperature and pressure within the experimental range using eq 1 and the parameters of Table 2. This equation should not be

used for extrapolation of the data outside the experimental conditions.

Finally it was determined that there exist a crossover in the solubility at 22 MPa and 308.15 K, 15MPa and 313.15 K, and 10 MPa and 323.15 K, respectively, between *p*- and *o*-coumaric acid. For *m*-coumaric acid, the solubilities tend to increase monotonically with increasing temperature and a crossover does not occur.

Literature Cited

Bartle, K. D.; Clifford, A. A.; Jafar, S. A. Solubilities of Solids and Liquids of Low Volatility in Supercritical Carbon Dioxide. *J. Phys. Chem. Ref. Data* **1991**, *20*, 713−757.

Casteele, K. V.; Geiger, H.; Sumere, C. E. V. Separation of phenols and coumarins by reverse-phase HPLC. *J. Chromatogr.* **1983**, *258*, 111−124.

Choi, Y. H.; Kim, J. W.; Noh, M. J.; Park, E. M.; Yoo, K.-P. Extraction of epicuticular wax and nonacosan-10-ol from *ephedra* herb utilizing supercritical carbon dioxide. *Korean. J. Chem. Eng.* **1996**, *13*, 216−219.

Noh, M. J.; Choi, E. S.; Kim, S. H.; Yoo, K.-P.; Choi, Y. H.; Chin, Y. W.; Kim, J. W. Supercritical Fluid Extraction and Bioassay Identification of Prodrug Substances from Natural Resources. *Korean J. Chem. Eng.* **1997**, *14*, 109−116.

Özcan, A. S.; Clifford, A. A.; Bartle, K. D. Solubility of Disperse Dyes in Supercritical Carbon Dioxide. *J. Chem. Eng. Data* **1997**, *42*, 590−592.

Yoo, K.-P.; Hong, I. K. Modeling of the Supercritical Fluid Extraction of Oilseeds. In *Supercritical Fluid Technology in Oil and Lipid Chemistry*; King, J. W., List, G. R., Eds.;AOCS Press: Champaign, IL, 1996; Chapter 6, pp 132−154.

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