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Solubilities of Flavone and 3-Hydroxyflavone in Supercritical Carbon Dioxide

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The solubilities of flavone and 3-hydroxyflavone in supercritical carbon dioxide (SC-CO_2) were measured at 308.2 K and 318.2 K over the pressure range from 9.1 MPa to 25.3 MPa by a flow type apparatus, which can detect the concentrations of the solutes in a supercritical fluid. The solubilities were determined from the mass of solute trapped by decompressing and the volume of CO_2. Solubility data were correlated by a solution model based on the regular solution model.

Introduction

Flavonoids such as flavone and 3-hydroxyflavone have been attracting much attention in pharmacology and related industries, because clinical and biological studies have indicated that flavonoids may play a significant role in the prevention of many forms of disease (Kimura et al., 1986). In general, flavonoids are included in the root of certain plants such as Scutellaria root. However, no effective extraction process from natural materials has been established on an industrial scale (Kitazaki et al., 1994; Mishima et al., 1996).

Supercritical fluid extraction (SFE) is expected to be a promising means of separating biologial substances from natural materials because of the mild conditions it provides. To aid design and optimization of SFE, solubilities of target substances in a supercritical fluid (SCF) are needed. In our previous work (Mishima et al., 1996), the possibility of extraction of flavonoids such as baicalein and baicalin from Scutellaria root was indicated by using supercritical carbon dioxide (SC-CO_2). And it was shown that flavonoids were able to be extracted from a natural matrix of plant efficiently without contamination. However, solubility data of flavonoids in SCF are limited.

In this work, the solubilities of flavone and 3-hydroxyflavone in SC-CO_2 at 308.2 K and 318.2 K over the pressure range from 9.1 MPa to 25.3 MPa were measured by a flow type apparatus. The chemical structures of flavone and 3-hydroxyflavone are shown in Figure 1. The solubilities of these substances were correlated by a solution model based on the regular solution model proposed by Ziger and Eckert (1983).

Experimental Section

Apparatus and Procedures. A flow type apparatus was used to measure the solubilities of flavone and 3-hydroxyflavone in SC-CO_2. A detailed description of the apparatus and operating procedures is given elsewhere (Iwai et al., 1991). The liquefied CO_2 leaving a gas cylinder was passed through a cooling unit to prevent vaporization of CO_2 from warming up and directed to a compressor which was capable of delivery pressure up to about 60 MPa and delivery rates up to 5.2 mL·min^{-1} (liquefied CO_2 basis). A back-pressure regulator was used to maintain a constant pressure with the pressure control accuracy of ±0.1 MPa. The equilibrium pressure was measured by a Bourdon gauge calibrated against a strain pressure gauge (accuracy ±0.3%). CO_2 passed through a preheating coil and then entered in two equilibrium cells placed with flavone or 3-hydroxyflavone. The cells were constructed from SUS316, and the inner diameter, height, and volume were 30 mm, 30 cm, and 210 cm^3, respectively. The solid component was packed in the second cell with glass beads to prevent channeling, while the first cell was used as a buffer tank. These cells were attached to a preheating coil and submerged in a water bath controlled with a temperature control accuracy of ±0.1 K. SCF saturated with the solid component was decompressed through an expansion valve and introduced into a U-shaped glass tube cooled in an ice bath. Gaseous CO_2 and the solid component was separated in the tube. The amount of the trapped solid component was determined by mass. The solute collected in the tubes was weighed by a direct reading balance (Exact A-V; accuracy 0.1 mg). The volume of CO_2 was measured by a wet-gas meter that was calibrated to an accuracy of ±0.4%. Usually, 0.1−0.3 g of solute was trapped, and the flow rate of expanded CO_2 was adjusted to 0.38−0.93 L·min^{-1} (gaseous CO_2 basis). A small amount of the solid remaining

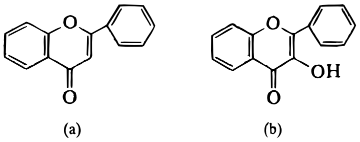

Figure 1. Chemical structures of flavone (a) and 3-hydroxyflavone (b).

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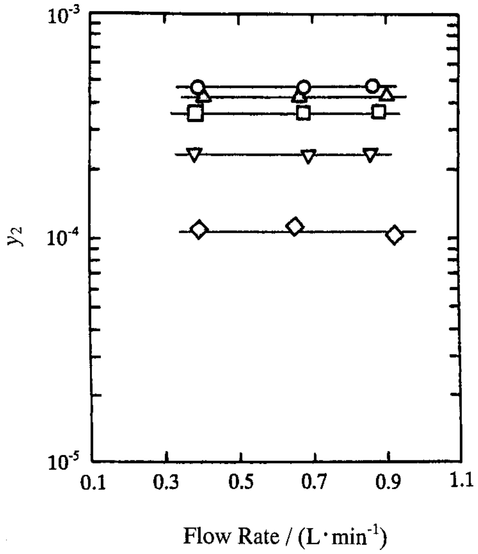

Figure 2. Relationship between the mole fraction solubility of flavone in SC-CO_2 at 308.2 K over the pressure range from 9.1 MPa to 25.3 MPa and the flow rate of expanded CO_2: (◇) 9.1 MPa; (▽) 10.2 MPa; (□) 15.2 MPa; (△) 20.3 MPa; (○) 25.3 MPa.

Table 1. Mole Fraction Solubilities y of Flavone and 3-Hydroxyflavone in SC-CO_2

flavone				3-hydroxyflavone			
$T = 308.2$ K		$T = 318.2$ K		$T = 308.2$ K		$T = 318.2$ K	
p/MPa	10^4y_2	p/MPa	10^4y_2	p/MPa	10^5y_2	p/MPa	10^5y_2
9.1	1.07	9.1	0.350	9.1	1.49	9.1	0.788
10.1	2.33	10.1	1.65	10.1	2.39	10.1	2.66
15.2	3.59	15.2	4.73	15.2	3.04	15.2	4.54
20.3	4.22	20.3	5.36	20.3	3.25	20.3	5.06
25.3	4.62	25.3	5.61	25.3	3.37	25.3	5.56

in the tube and the expansion valve was removed and trapped by using SC-CO_2 through a bypass line.

Materials. Flavone and 3-hydroxyflavone were supplied by Wako Pure Chemical Industries Ltd. Their purities were believed to be more than 98 and 99%, respectively. High-purity CO_2 (more than 99%, Fukuoka Sanso Co. Ltd.) was used as received.

Results and Discussion

The measurements were carried out for several flow rates of CO_2 at known pressures, as shown in Figure 2. The solubilities of flavone were independent of the flow rate of expanded CO_2, where the condition of CO_2 is standard state temperature and pressure. Similar results were obtained for 3-hydroxyflavone. This shows that the solubilities of flavonoids were measured under equilibrium conditions in the flow type apparatus. The reproducibility of these solubilities was within ±4.0% when the pressure was varied from 9.1 MPa to 25.3 MPa. The experimental values listed in Table 1 were obtained from an arithmetic average of several measurements at each pressure. Experimental data of flavone and 3-hydroxyflavone at 308.2 K and 318.2 K are given in Figures 3 and 4. These figures show the temperature and pressure effects on solubility. Just above the critical pressure of CO_2, the solubilities of flavone and 3-hydroxyflavone drastically increase because of a rapid increase in density with pressure. For pressures above the critical point of the solvent up to nearly 10 MPa, the solubility decreases as the temperature increases. For pressures above 10 MPa, the solubility increases with increasing temperature because the decrease in CO_2 density cannot overcome the increase in vapor pressure.

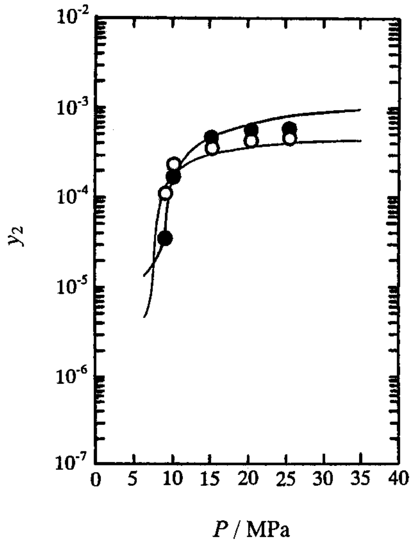

Figure 3. Mole fraction solubilities of flavone in SC-CO_2: (○) experimental data at 308.2 K; (●) experimental data at 318.2 K; (—) calculated results.

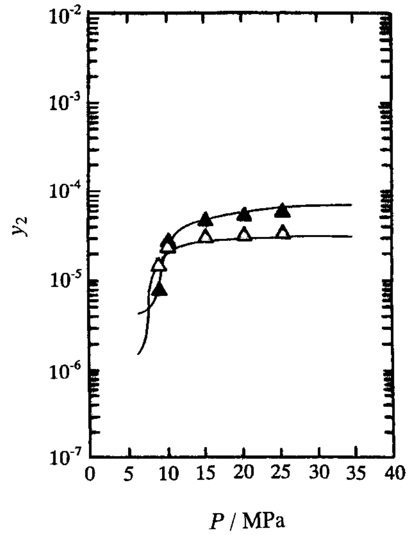

Figure 4. Mole fraction solubilities of 3-hydroxyflavone in SC-CO_2: (△) experimental data at 308.2 K; (▲) experimental data at 318.2 K; (—) calculated results.

To confirm the reliability of the experimental data, the enhancement factor, $E = py_2/p_2^{sat}$ (Brennecke and Eckert, 1989), was plotted against the density of pure CO_2, ρ_1, where y_2 is the solubility of the solid component in the SCF and p is the equilibrium pressure. The saturated vapor pressure, p_2^{sat}, was calculated by the modified Abrams–Massaldi–Prausnitz (AMP) equation (Sakoguchi et al., 1991), where the AMP equation is derived by Abrams et al. (1974), extending a suggestion based on a kinetic theory by Moelwyn-Hughes (1961). Furthermore, Macknick and Prausnitz (1979) showed that a group-contribution method for predicting the vapor pressure of hydrocarbons and hydrocarbons containing nitrogen and sulfur moieties would be applicable to the AMP equation. However, not all group parameters s, E_0/R, and V_W in the AMP equation for high-boiling compounds are determined. So Sakoguchi et al. (1991) proposed the modified AMP equation which was able to predict the group parameters from molecular structures of flavonoids. The density of CO_2 was calculated by the five-parameter van der Waals type cubic equation of state with the optimized parameters (Adachi et al., 1986). As shown in Figures 5 and 6, it was observed that the logarithm of the enhancement factor, ln E, was a good

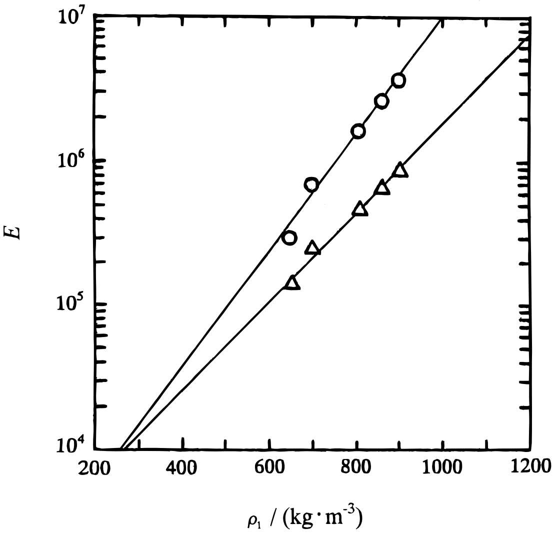

Figure 5. Relationship between the enhancement factor E and density of pure CO$_2$ ρ_1: (○) flavone at 308.2 K; (△) 3-hydroxyflavone at 308.2 K; (—) results calculated by eq 1.

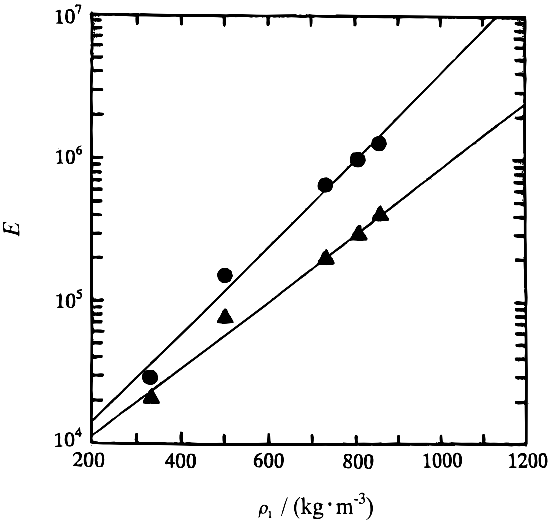

Figure 6. Relationship between the enhancement factor E and density of pure CO$_2$ ρ_1: (●) flavone at 318.2 K; (▲) 3-hydroxyflavone at 318.2 K; (—) results calculated by eq 1.

Table 2. Coefficients of Eq 1

solute	T/K	A	10^3B/m^3·kg^{-1}
flavone	308.2	6.641	9.405
	318.2	10.38	7.139
3-hydroxyflavone	308.2	6.114	7.046
	318.2	9.431	5.413

linear function of the solvent density, ρ_1, for each component. The relationship can be represented by the following equation:

$$\ln E = A + B\rho_1 \tag{1}$$

where coefficients A and B are given in Table 2.

Correlation

Ziger and Eckert (1983) have assumed that the solubility of the solid component in SCF is expressed by a solution model based on the regular solution model:

$$\ln E = \eta\left[\frac{\nu_2^{\,s}(2\delta_1\delta_2 - \delta_1^{\,2})}{RT} - \ln\left(1 + \frac{\delta_1^{\,2}}{p}\right)\right] + \upsilon \tag{2}$$

Table 3. Physical Properties of Flavone and 3-Hydroxyflavone

			$10^3p_2^{\rm sat}$/Pa	
substance	$10^3\nu_2^{\rm s}$/ m^3·mol^{-1}	δ_2/ MPa$^{1/2}$	T = 308.2 K	T = 318.2 K
flavone	0.1765[a]	24.47[b]	3.361[c]	10.96[c]
3-hydroxyflavone	0.1823[a]	27.63[b]	0.9926[c]	3.441[c]

[a] Estimated by the relation $\nu_2^{\rm s} = 1.5V_{\rm W}$ where $V_{\rm W}$ is given by Bondi method. [b] Estimated by the Fedors method. [c] Estimated by the modified AMP equation.

Table 4. Optimized Values of η and ν in Eq 2 and Deviations

substance	η	ν	100σ[a]
flavone	0.9477	7.687	19
3-hydroxyflavone	0.6169	7.975	15

[a] $\sigma = (1/N)\Sigma|y_{\rm exp} - y_{\rm calc}|/y_{\rm exp}$, where N is the number of data.

where T is the absolute temperature, R is the universal gas constant, δ_1 is the solubility parameter of SC-CO$_2$ calculated by the method proposed by Giddings et al. (1968), p is the experimental pressure, δ_2 is the solubility parameter of the solid component calculated by the Fedors method (Fedors, 1974), $\nu_2^{\rm s}$ is the molar volume of the solid component, η and υ are the parameters defined by eq 2, respectively. $\nu_2^{\rm s}$ is nearly proportional to the hard-core van der Waals volume, $V_{\rm W}$, which was obtained by the method of Bondi (1968). As shown by Yamamoto et al. (1987), we assumed that the proportionality constant, $K = \nu_2^{\rm s}/V_{\rm W}$, was about 1.5. So the $\nu_2^{\rm s}$ for flavone and 3-hydroxyflavone was calculated with their values of $V_{\rm W}$ and $K = 1.5$. The physical properties of flavone and 3-hydroxyflavone are shown in Table 3. The values of η and υ can be calculated by using a generalized linear least-squares approach. They are listed in Table 4. The logarithm of the enhancement factor has been correlated well by the regular solution model. The solubilities of flavone and 3-hydroxyflavone in SC-CO$_2$ can also be well represented, as shown in Figures 3 and 4.

Conclusion

The solubilities of flavone and 3-hydroxyflavone in SC-CO$_2$ were measured by using a flow type apparatus at 308.2 K and 318.2 K over the pressure range from 9.1 MPa to 25.3 MPa. Furthermore, the solubilities of these substances in SC-CO$_2$ have been correlated by using a solution model based on the regular solution model. It was shown that the solubilities of these substances can be correlated with fairly good accuracy.

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