Solubility of Syringic and Vanillic Acids in Supercritical Carbon Dioxide

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The solubility in supercritical carbon dioxide, at pressures from (10 to 50) MPa and temperatures from (40 to 60) °C, is reported for two nonflavonoid, low molecular weight phenolic compounds, 4-hydroxy-3,5-dimethoxybenzoic acid (syringic acid) and 4-hydroxy-3-methoxybenzoic acid (vanillic acid). Two types of models have been used for correlation of the experimental solubility data. First a rigorous thermodynamic method, with the Peng−Robinson equation of state, was used to determine the fugacity of the fluid phase. Second, two semiempirical density-dependent correlations were used: a linear correlation between the enhancement factor and the density of the solvent, as suggested by Schmitt and Reid, and the Chrastil correlation.

Introduction

A variety of phenolic compounds are found in most vegetables. Second only to carbohydrates, they are the most abundant type of compounds among plants. The interest in these phenolic compounds lies in their known health benefits due to their antioxidant activity and ability as free-radical scavengers. These properties give them great potential as active principles in the pharmaceutical industry and as antioxidants in the food industry. There is, therefore, an increasing interest in isolating these compounds from their natural matrices. One of the separation technologies that is being explored to achieve such isolation is supercritical fluid extraction (SFE). SFE is under consideration for separation of natural substances from complex materials due to the mild conditions needed and other environmental benefits.[1]

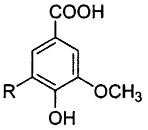
The efficient design of any particular SFE process requires a knowledge of the solute's solubility. In this work, the solubility in supercritical CO_2, at pressures from (10 to 50) MPa and temperatures from (40 to 60) °C, is presented for two nonflavonoid, low molecular weight phenolic compounds, 4-hydroxy-3,5-dimethoxybenzoic acid (syringic acid) and 4-hydroxy-3-methoxybenzoic acid (vanillic acid). These two compounds present a Trolox equivalent antioxidant activity[2] (TEAC) of 1.4 mM. The TEAC is defined as the concentration of Trolox (the water-soluble vitamin E analog) solution with an antioxidant potential equivalent to a 1 mM concentration of the compound under consideration.

Stassi et al.[3] have previously reported the solubility of vanillic acid in supercritical (SC) CO_2 for two isotherms, 313 K and 328 K, covering a pressure range from (8.6 to 25) MPa. In this work, the pressure range has been widened up to 50 MPa and two new isotherms have been measured. Correlation of the experimental solubility data has been carried out by using two types of methods: a thermodynamically rigorous method,[4] where the fugacity of the fluid phase was calculated by means of the Peng−Robinson equation of state (PR-EOS), and two semiempirical density-dependent correlations. One of them was a linear correlation between the enhancement factor and the density of the solvent, as suggested by Schmitt and Reid,[5] and the second one was the Chrastil correlation.[6] These semiempirical correlations are widely used, and although they cannot predict unknown phase equilibria, they are useful tools for experimental data correlation.

Table 1. Physical Properties of the Solutes

solute	syringic acid	vanillic acid
formula	$C_9H_{10}O_5$	$C_8H_8O_4$
R group	OCH_3	H
MW	198.18	168.15
mp (101.33 kPa)/K[a]	480 ± 2	483 ± 2
T_b (101.33 kPa)/K[b]	712.9	840.5
T_c/K[b]	941.40	1105.67
p_c/MPa[b]	4.02	4.52
ω[b]	1.190	1.302

chemical structure of syringic and vanillic acids



[a] Sigma database (www.sigma-aldrich.com/saws.nsf/msdshelp).
[b] Estimated by the Joback method implemented in PE.[7]

Experimental Section

Chemicals. The solutes used in this work, syringic and vanillic acids, were supplied by Sigma, (>98% purity). The molecular weight (MW) and normal melting point (mp) of these solutes are reported in Table 1 together with the estimated normal boiling point (T_b), critical temperature (T_c), and pressure (p_c), and acentric factor (ω). The main chemical structure of these compounds is represented next to Table 1 where the identity of the R group for the two compounds is given.

The carbon dioxide used as supercritical solvent (SFC/SFE quality) was supplied by Air Liquide. HPLC-grade methanol and acetonitrile (Lab-Scan) and puriss. p.a. (98%) formic acid (Fluka) were used as solvents for sample analyses. Glass beads in a 30/60 mesh (Phase Separations) were used to distribute the solute in the equilibrium cell, and glass wool (Panreac) was placed at the top of each of the three stages of the equilibrium cell to prevent solid entrainment.

Apparatus and Procedures. The solubility of the solids was experimentally determined by the dynamic analytical

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Table 2. Experimental Solubility Data of Syringic and Vanillic Acids in Supercritical Carbon Dioxide: Pressure *p*, Temperature *T*, SC CO_2 Density at Each *p* and *T* $\rho(CO_2)$, Solubility Expressed as Solute Mol Fraction *y*, and Standard Error of Each Solubility Datum SE

		syringic acid		vanillic acid	
T/K	p/MPa	$y \times 10^7$	SE $\times 10^7$	$y \times 10^7$	SE $\times 10^7$
313	8.5			14.34	1.45
	10	3.15	0.08	35.46	2.72
	15	12.21	0.14	85.19	1.53
	20	18.74	0.29	114.66	2.99
	25	24.94	0.38	151.25	4.02
	30	30.09	0.41	167.48	5.24
	35	37.76	0.93	183.42	9.10
	40	44.70	1.91	226.31	7.11
	45	48.92	2.44	243.93	7.88
	50	56.41	2.60	260.01	9.73
323	10	0.58	0.02	16.88	1.16
	15	12.60	0.22	85.67	3.94
	20	26.06	1.06	157.09	3.96
	25	38.57	1.29	204.93	8.17
	30	44.59	2.25	254.47	9.57
	35	58.52	0.83	296.53	9.27
	40	69.53	1.61	346.31	4.14
	45	80.06	2.24	363.84	7.86
	50	92.14	3.12	389.23	5.45
333	10	0.01	0.00	9.37	0.66
	15	15.50	0.02	86.74	2.25
	20	30.34	0.04	193.94	1.52
	25	44.68	2.07	264.86	8.51
	30	60.67	2.27	338.61	5.55
	35	75.59	2.16	391.64	17.13
	40	96.29	2.79	474.23	16.89
	45	111.06	3.33	555.36	17.60
	50	127.09	4.26	607.10	17.88

method in an apparatus that has been previously described and used in our laboratory to obtain reliable solubility data of solid solutes in SC CO_2.[8,9] The equilibrium cell was filled with the solute (~200 mg) distributed on glass beads in order to improve the solute−solvent contact and avoid channeling when the SC solvent passes through them. The solvent flow was kept low enough (around 0.5 L/min under normal conditions) to achieve solvent saturation before exiting the equilibrium cell. The equilibrium cell was kept at the desired temperature (±0.1 K) in an oven provided with a thermal regulator and at the desired pressure by means of a back-pressure regulator (Tescom Co., model 26-1721) that allowed pressure to be controlled with an accuracy of ±1% of relief pressure range. A 5-μm inline filter and a column packed with stainless steel balls were used for solute trapping after CO_2 depressurization. Filter and trap were rinsed repeatedly with an 80% methanol aqueous solution in order to collect the solute quantitatively and have the sample ready for analysis. The depressurized CO_2 was quantified with a totalizer flow meter.

Sample analysis was carried out offline by using a high-performance liquid chromatograph equipped with a diode array detector (DAD, Hewlett-Packard 1100 series). The coupling of chromatography and DAD would allow the detection of the compound degradations that could take place or some of the impurities of the pure solute that could be preferentially solved by the SC CO_2. None of those was the case of the solutes studied in this work. Quantification was made at a wavelength of 280 nm for syringic acid and 260 nm for vanillic acid with the calibration curves previously obtained for each compound in the range where the Lambert−Beer law was valid.

The experimental solubility was determined by carrying out at least 5 experiments in which the total amount of SC CO_2 that flowed through the cell was varied, hence varying the total amount of solute dissolved. The plot of the amount of solute dissolved vs the amount of CO_2 used to dissolve it is a linear function whose slope is the solubility at the temperature and pressure at which the operation was carried out. The standard error (SE) given next to every solubility datum in Table 2 indicates the quality of the linear fit.

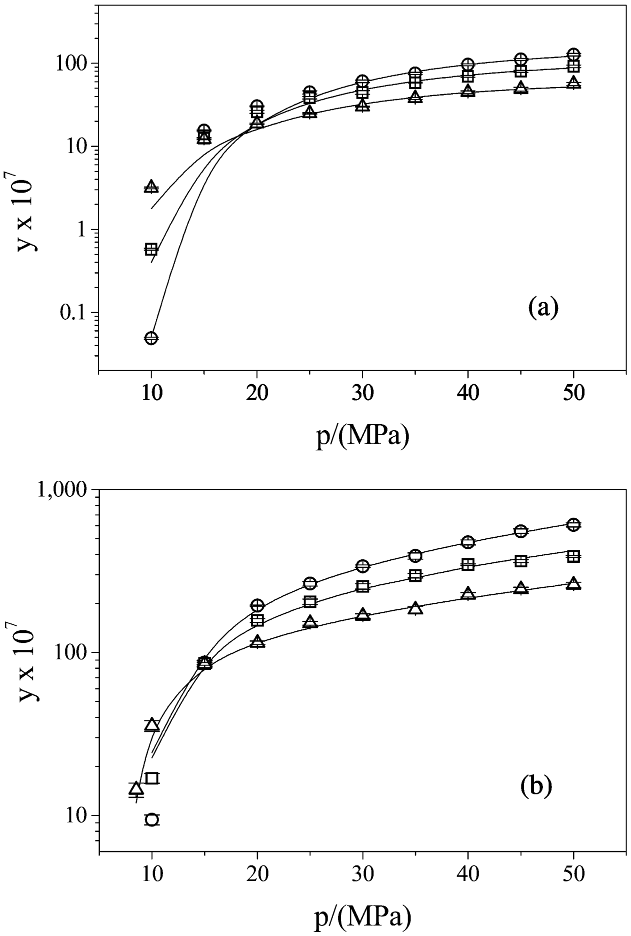

Figure 1. Experimental solubility of syringic acid (a) and vanillic acid (b) in SC CO_2: △, 313 K; □, 323 K; ○, 333 K. The error bars represent the standard error of each solubility datum; continuous lines represent the solubility isotherms calculated with the PR-EOS.

Results and Discussion

The experimental solubility data of syringic acid and vanillic acid in SC CO_2, at different conditions of pressure, *p*, and temperature, *T*, are presented in Table 2 and plotted in Figure 1, together with their standard errors. The temperatures studied range from (313 to 333) K and the pressures from (8.5 to 50) MPa.

The results show that the solubility increased with pressure, at constant temperature, in all cases. The effect of temperature is more complex, and retrograde solubility (crossover pressure) behavior[5] can be observed for both acids. At pressures below the crossover pressure, the solubility decreases with increasing temperature due to the dominant effect of the density decrease, while at pressures above the crossover pressure, the solubility increases with temperature primarily because of the increasing vapor pressure of the solid with increasing temperature. Such retrograde behavior has been reported before for different organic compounds.[10]

Table 3. Results of the Solubility Data Correlation through the PR-EOS: Number of Data Points Used in the Correlation *n*, Binary Interactions Parameters k_{ij} and l_{ij}, and Percentage of Average Absolute Relative Deviations AARD

			parameters of PR-EOS		
solute	*n*	*T*/K	k_{ij}	l_{ij}	AARD/%
syringic acid	9	313	0.0670	−0.1575	11.05
	9	323	0.0575	−0.1783	14.78
	9	333	0.0493	−0.1973	13.41
vanillic acid	10	313	0.5086	0.4396	2.44
	9	323	0.5250	0.4856	5.30
	9	333	0.5171	0.4735	4.98

Table 4. Results of the Solubility Data Correlation Considering a Linear Dependence between the Enhancement Factor and the Density of the Solvent ($\ln E = A + B\rho$): Number of Data Points Used in the Correlation *n*, Parameters *A* and *B*, Percentage of Average Absolute Relative Deviations AARD, and R^2

				correlation parameters			
solute	*n*	pressure range/ MPa	*T*/K	*A*	$B/(10^2\ \mathrm{m^3/kg})$	AARD/%	R^2/%
syringic acid	9	10−50	313	11.95	1.231	5.62	99.79
	9	10−50	323	11.24	1.117	3.93	99.94
	9	10−50	333	7.94	1.417	32.13	97.24
vanillic acid	10	8.5−50	313	31.50	0.782	24.83	98.06
	9	10−50	323	28.82	0.850	14.94	98.56
	9	10−50	333	26.50	0.897	7.46	99.79

Under the same conditions of temperature and pressure, vanillic acid shows higher solubility than syringic acid. This may be due to the lower molecular weight of vanillic acid and its smaller polarization since the solvent, carbon dioxide, is nonpolar.

According to the most rigorous methods for modeling-phase equilibrium data, the solubility of the solid solute in the SCF can be calculated by means of eq 1, which considers a solid phase, formed by the pure solute (2), in equilibrium with a fluid phase (here considered as a dense gas) formed by a mixture of solvent (1) and solute (2)[4]

$$y_2 = \frac{p_2^{\mathrm{s}}}{p}\frac{\phi_2^{\mathrm{s}}}{\phi_2}\exp\left[\frac{v_2^{\mathrm{s}}(p - p_2^{\mathrm{s}})}{RT}\right] \qquad (1)$$

where p_2^{s} is the saturation (vapor) pressure of the pure solid, ϕ_2 is the fugacity coefficient at the system pressure p, ϕ_2^{s} is the fugacity coefficient at saturation pressure p_2^{s}, and v_2^{s} is the solid molar volume, all at the system temperature T.

The PR-EOS, whose parameters for the mixture have been calculated according to the quadratic mixing rules,[4] has been used for calculating the fugacity coefficients. The PR-EOS gives good quantitative fits for a wide variety of systems, but critical properties (T_c and p_c) and the acentric factor (ω) of solute and solvent are needed for calculating the EOS parameters for the pure components. These properties are available for CO_2 but not for the solids that are the subject of this work; therefore, they have been estimated by the Joback[11] group contribution method and are listed in Table 1. This group contribution method has also been used for prediction of the normal boiling temperature of the solutes.

The interaction binary parameters k_{12} and l_{12} of the PR-EOS have been obtained by fitting the experimental solubility data to eq 1. The regression procedure was carried out by minimizing the average absolute relative deviation (AARD) between experimental (y_{exp}) and calculated (y_{cal}) solubility data (eq 2), using the Phase Equilibria 2000 (PE 2000) program developed by Prof. Brunner's group[7]

$$\mathrm{AARD}\ (\%) = \left(\frac{100}{n}\right)\sum\frac{|y_{\mathrm{exp}} - y_{\mathrm{cal}}|}{y_{\mathrm{exp}}} \qquad (2)$$

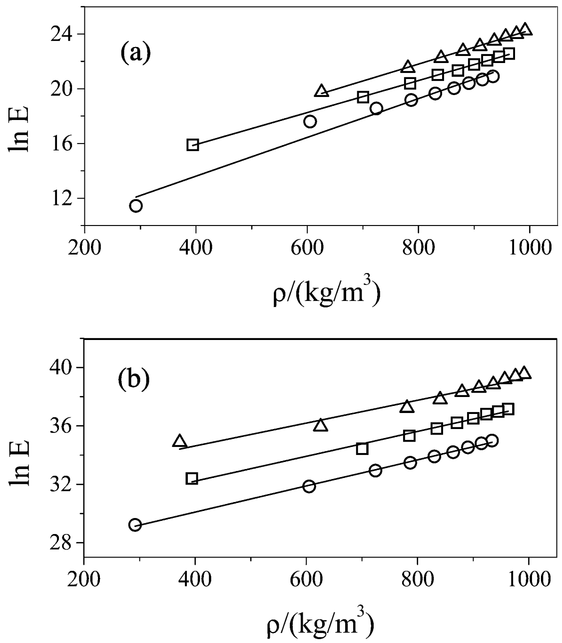

Figure 2. Experimental solubility of syringic acid (a) and vanillic acid (b) in SC CO_2: △, 313 K; □, 323 K; ○, 333 K. Continuous lines represent the solubility isotherms calculated with the enhancement factor model.

The values of the interaction parameters k_{12} and l_{12} for the different temperatures are listed in Table 3 together with the corresponding AARD values. The solubility curves as predicted by eq 1 and the PR-EOS are represented by continuous lines in Figure 1, where it may be observed that the model closely reproduces the experimental solubilities far above the critical pressure of the solvent, while larger errors are found close to it. This may be due to the large scatter that experimental solubility data usually present in the vicinity of the critical point as a consequence of the high sensitivity that density presents to pressure.

Two semiempirical models have also been used for data correlation. The first one, proposed by Schmitt and Reid,[5] assumes a linear functionality between the logarithm of the enhancement factor ($\ln E$), as calculated from eq 3, and the density of the solvent, ρ

$$E = y_2 p / p_2^{\mathrm{s}} \qquad (3)$$

The enhancement factor provides a measure of the extent that pressure enhances the solubility of the solid in the gas, and it is always greater than unity. The vapor pressure of the solid, necessary to calculate the enhancement factor using eq 3, has been estimated according to the method proposed by Grain.[11] The density of the solvent was obtained from Span and Wagner.[12] This enhancement factor model is very useful for data correlation because of its simplicity and good fitting results. The results of data correlation to this model are presented in Table 4 and Figure 2. Table 4 includes the AARD between experimental and calculated solubility, y, and R^2 that indicates the variability in the dependent variable ($\ln E$) explained by the model.

Table 5. Results of the Solubility Data Correlation by the Chrastil Model: Number of Data Points Used in the Correlation *n*, Parameters of Chrastil Equation *k*, *a*, and *b*, Percentage of Average Absolute Relative Deviations AARD, and R^2

			parameters of the Chrastil equation				
solute	*n*	pressure range/MPa	*k*	*a*	*b*	AARD/%	R^2/%
syringic acid	27	10−50	7.264	−6534	−32.93	10.50	98.87
vanillic acid	28	8.5−50	4.335	−4931	−16.57	13.49	97.92

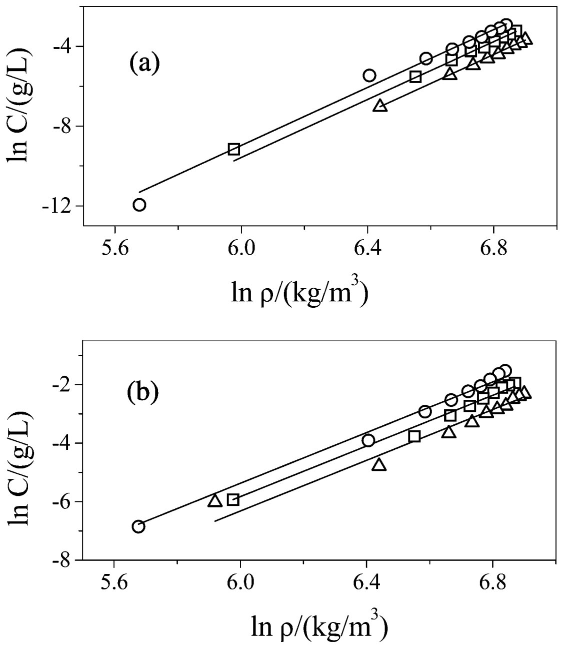

Figure 3. Experimental solubility of syringic acid (a) and vanillic acid (b) in SC CO_2: △, 313 K; □, 323 K; ○, 333 K. Continuous lines represent the solubility isotherms calculated with the Chrastil model.

The second empirical correlation used, the Chrastil correlation,[6] assumes the formation of a solvation complex between molecules of the SC solvent and the solute at equilibrium. This model leads to a linear relationship between the solubility of the solute, C, expressed as (g of solute)/(L of solvent) and the density of the solvent, ρ, in g L^{-1}, for a given temperature (in K) as follows

$$\ln C = k \ln \rho + a/T + b \tag{3}$$

a, b, and k are the adjustable parameters of the model. The Chrastil equation has the advantage of having only three parameters to fit all the experimental data, no matter at which temperature they were obtained. Moreover, this equation does not require the estimation of the properties of the pure components.

The parameters a, b, and k were obtained by nonlinear regression of the experimental data using the Marquardt algorithm and are reported in Table 5 together with the AARD between experimental and calculated solubility, C. The quality of the correlation is indicated by R^2 that indicates the variability in the logarithm of the solubility ($\ln C$) explained by the model. The plots of the experimental data and the solubility isotherms calculated with the Chrastil model are presented in Figure 3, where the quality of the correlations can be visually evaluated.

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