SOLUBILITY OF SYRINGIC AND VANILLIC ACIDS IN SUPERCRITICAL CARBON DIOXIDE

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1. INTRODUCTION

Phenolic compounds are a wide and heterogeneous group of substances that are widely distributed in vegetables. They are so abundant among superior plants, that only carbohydrates are on top of them. The interest of these phenolic compounds lies on their known health benefits due to their antioxidant activity and to their ability as free radical scavengers. These properties give them a 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. However, most of them are thermolabile and some extraction technology that not requires high temperatures should be used. One of the technologies that is being explored is supercritical fluid extraction (SFE), that is becoming an extended operation 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 needs the previous knowledge of the solutes solubility. In this work, the solubility of two non-flavonoid, low molecular weight phenolic compounds, 4-hydroxy-3,5-dimethoxybenzoic acid (syringic acid) and 4-hydroxy-3-methoxybenzoic acid (vanillic acid), in supercritical CO_2, at pressures from 10 to 50 MPa and temperatures from 40 to 60ºC, is presented. These two compounds present a Trolox equivalent antioxidant activity (TEAC) of 1.4 mM [2]. 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.

Two types of models have been used for correlation of the experimental solubility data: a rigorous thermodynamic method [3] where the Peng-Robinson equation of state (PR-EOS) was used to determine the fugacity of the fluid phase, and two semiempirical density dependent correlations: a linear correlation between the enhancement factor and the density of the solvent, as suggested by Schmitt and Reid [4], and the Chrastil correlation [5]. These semiempirical correlations are widely used and, although they are not capable of predicting unknown phase equilibria, they are useful tools for experimental data correlation

2. EXPERIMENTAL

2.1. 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 R group for each compound is given.

Table 1: Physical properties of the solutes.

Solute	Syringyc 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	1.3016
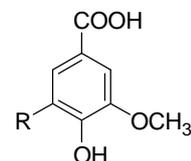
[a] Sigma data base (www.sigma-aldrich.com/saws.nsf/msdshelp).
[b] Estimated by the Joback method implemented in PE [6].

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 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.

2.2. Apparatus and procedure

The solubility of the solids was experimentally determined by the dynamic analytical method in an apparatus that has been previously described and used in our laboratory to obtain solubility data of solid solutes in SC-CO_2 [7, 8].

Sample analysis was carried out off-line by using an HPLC equipped with a diode array detector (DAD) (Hewlett-Packard 1100 series). The coupling of chromatography and DAD would allow to detect 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 with 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.

3. RESULTS AND DISCUSSION

The experimental solubility data of vanillic acid and syringic acid in SC-CO_2, at different conditions of pressure, p, and temperature, T, are 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 [4] can be observed for both acids. At pressures above the crossover pressure, the solubility increases with temperature while at pressures below the crossover pressure, the solubility decreases with increasing temperature.

Under the same conditions of temperature and pressure, vanillic acid shows higher solubility than syringic acid which may be due to the larger polarization of the syringic acid molecule that has a methoxy group more than the vanillic acid molecule.
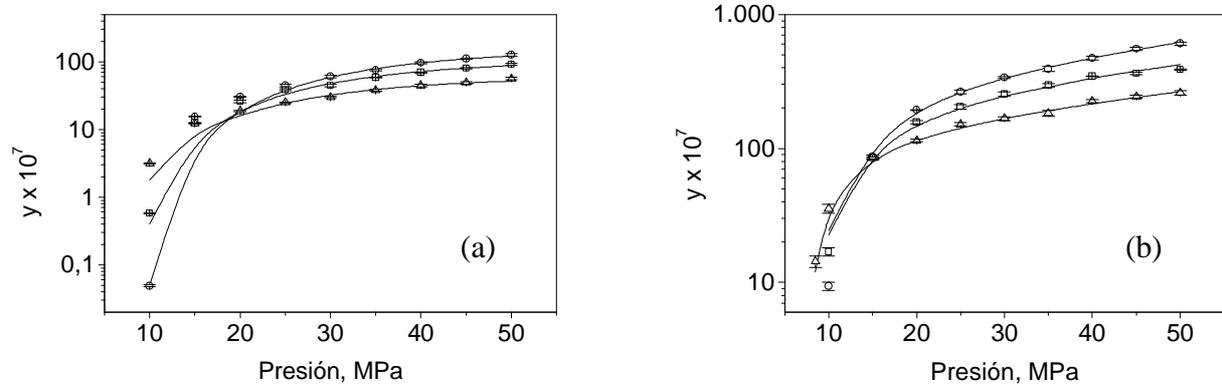
Figure 1: Experimental solubility of syringic acid (a) and vanillic acid (b) in SC-CO$_2$. ($\triangle$) 313 K, (?) 323 K, (?) 333 K. The error bars represent the standard error of each solubility data. Continuous lines represent the solubility isotherms calculated with the PR-EOS.

According to the most rigorous methods for modeling 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*) [3].

$$y_2 = \frac{p_2^s}{p} \frac{f_2^s}{f_2} exp\left[\frac{u_2^s\left(p - p_2^s\right)}{RT}\right]$$
(1)

In eq.(1), p_2^s is the saturation (vapor) pressure of the pure solid, f_2 the fugacity coefficient at the system pressure p, f_2^s the fugacity coefficient at saturation pressure p_2^s, and u_2^s the solid molar volume, all at the system temperature T.

The Peng Robinson equation of state (PR-EOS), whose parameters for the mixture have been calculated according to the quadratic mixing rules [3], 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 subject of this work; Therefore, they have been estimated by the Joback group contribution method [6] 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, using the Phase Equilibria 2000 (PE 2000) program developed by Prof. Brunner´s group [6].

The values of the interaction parameters k_{12}, and l_{12} for the different temperatures are listed in Table 2 together with the corresponding AARD values. The solubility curves as predicted by

Eq. (1) and the PR-EOS are represented by continuous lines in Fig. 1, where it may be observed that the model reproduces fairly well 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.

Table 2: 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.

Solute	n	T/K	Parameters of PR-EOS		
			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

Two semiempirical models, have also been used for data correlation. The first one, proposed by Schmitt and Reid [4] assumes a linear functionality between the logarithm of the enhancement factor (ln E), as calculated from Eq. (2), and the density of the solvent, ρ.

$$E = y_2 \cdot p / p_2^s \tag{2}$$

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. (2), has been estimated according to the method proposed by Grain [9]. The enhancement factor model is very useful for data correlation because of its simplicity and good fits. The results of data correlation to this model are presented in Fig 2 and Table 3. It may be observed in Table 3, that the model reproduces much better the experimental data when the parameters are obtained without including the solubilities obtained at pressures in the vicinity of the critical point of carbon dioxide.
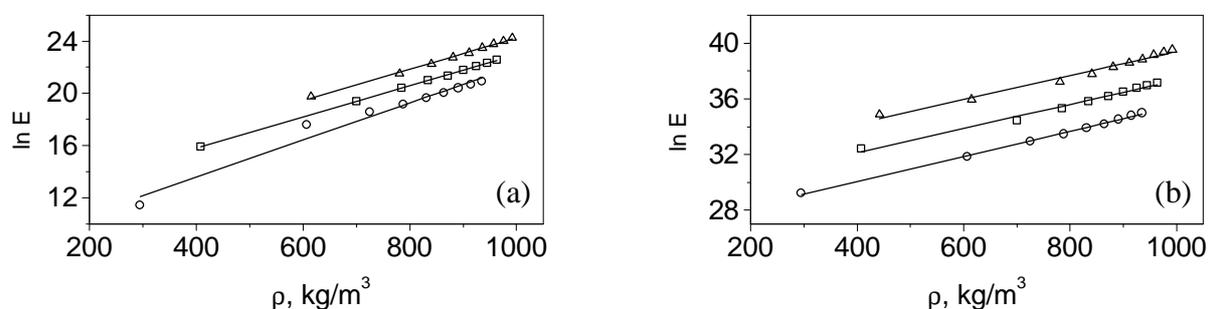
Figure 2: Experimental solubility of syringic acid (a) and vanillic acid (b) in SC-CO$_2$. ($\triangle$) 313 K, (?) 323 K, (?) 333 K. Continuous lines represent the solubility isotherms calculated with the enhancement factor model.

Table 3: Results of the solubility data correlation considering a linear dependence between the enhancement factor and the density of the solvent ($ln\,E = A + B\mathbf{r}$): number of data points used in the correlation, n, parameters A and B, percentage of average absolute relative deviations, AARD, and s-squared, s^2.

| Solute | n | Pressure range/MPa | T/K | Correlation Parameters | | | |
				A	$B/(10^2\ m^3/kg)$	AARD (%)	s^2
Syringic acid	9	10-50	313	12.25	1.20	7.86	0.9960
	9	10-50	323	11.00	1.20	2.30	0.9997
	9	10-50	333	7.88	1.42	33.60	0.9723
	8*	15-50	333	11.24	1.02	9.15	0.9914
Vanillic acid	9	8.5-50	313	30.77	0.863	16.06	0.9842
	8*	10-50	313	29.79	0.972	10.38	0.9892
	8	10-50	323	28.64	0.871	12.97	0.9885
	8	10-50	333	26.47	0.901	7.35	0.9980

* correlations excluding the solubility data obtained at pressures in the vicinity of the critical point of carbon dioxide.

The second empirical correlation used, was the Chrastil correlation [5] that assumes the formation of a solvato 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, $\textit{?}$, in g/L, for a given temperature (in K) as follows:

$$ln\,C = k \cdot ln\,\mathbf{r} + a/T + b \tag{3}$$

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 4 together with the AARD between experimental and calculated solubility, C. The quality of the correlation is indicated by s-squared. A plot of the experimental data and the solubility isotherms calculated with the Chrastil model is presented in Fig. 3 where the quality of the correlation can be visually evaluated.

Table 4: Results of the solubility data correlation by the Chrastil model: number of data points used in the correlation, n, parameters of Chrastil equation, a, b and k, percentage of average absolute relative deviations, AARD, and s-squared, s^2.

| Solute | n | Pressure range/MPa | Parameters of the Chrastil equation | | | | |
			k	a	b	AARD (%)	s^2
Syringic acid	27	10-50	7.411	-6495	-34.05	10.73	0.9896
Vanillic acid	28	8.5-50	4.641	-5426	-17.11	9.43	0.9928
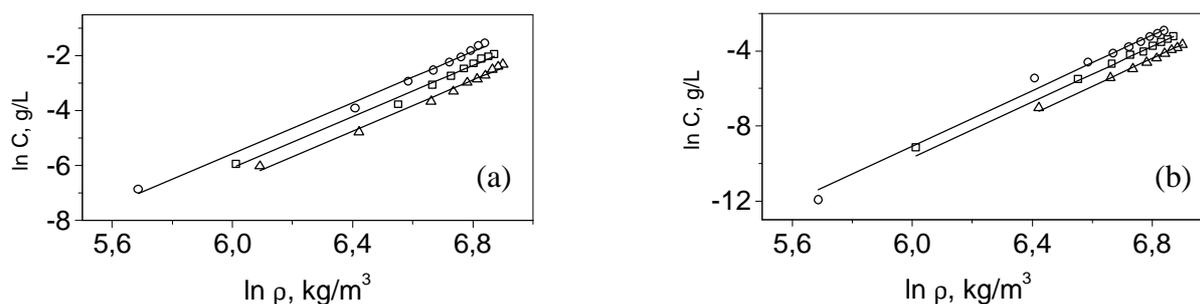
Figure 3: Experimental solubility of syringic acid (a) and vanillic acid (b) in SC-CO$_2$. ($\triangle$) 313 K, (?) 323 K, (?) 333 K. Continuous lines represent the solubility isotherms calculated with the Chrastil model.

ACKNOWLEDGMENTS

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