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Solubility of protocatechuic acid, sinapic acid and chrysin in supercritical carbon dioxide

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ABSTRACT

Solubility data of some phenolic compounds of industrial interest, such as protocatechuic acid (3,4-dihydroxybenzoic acid), chrysin (5,7-dihydroxyflavone) and sinapic acid (3,5-dimethoxy-4-hydroxycinnamic acid) in supercritical carbon dioxide were determined at pressures of 200, 300 and 400 bar and temperatures of 40, 50 and 60 °C. Experimental data were correlated with semi-empirical Chrastil model and thermodynamic modeling using the Peng–Robinson equation of state with classical mixing rule. The critical properties, acentric factor, and vapor pressure of these compounds were estimated by group contribution methods. The solubility values followed a similar tendency, with higher solubility with increasing temperature and pressure, and no crossover pressure in the range studied. However, a crossover pressure around 150 bar was observed when extrapolating the solubility data by the Chrastil equation, which is in agreement with values reported in the literature for phenolic compounds, thereby indicating the consistency of the solubility experimental data.

1. Introduction

Many health benefits have been attributed to phenolic compounds, which are secondary plant metabolites [1]. Protocatechuic acid (3,4-dihydroxybenzoic acid) is a phenolic acid widely found in fruits and vegetables. High amounts of protocatechuic acid were quantified in açai [2], mango [3], grapes [4], and green propolis [5], and in plants, such as *Indigofera hirsuta* [6], *Camelina sativa* seeds [7] and *Scutellaria barbata* [8] used in traditional Chinese medicine. Furthermore, protocatechuic acid has positive effects against carcinogenesis [9]. Chrysin (5,7-dihydroxyflavone) is a flavonoid found in honey [10], green propolis [11] and passion fruit (*Passiflora incarnata*) [12]. It has antioxidant activity, anti-inflammatory, anti-diabetic [13] and anticancer effects [14]. Sinapic acid (3,5-dimethoxy-4-hydroxycinnamic acid) is a derivative of cinnamic acid, available on rye extract (*Secale cereale* L.) [15] and red propolis [16], with neuroprotective effects [17] and anti-inflammatory activity [18].

Natural extracts rich in phenolic compounds can be obtained by extraction with supercritical carbon dioxide ($scCO_2$), which is a GRAS safe solvent (Generally Recognized As Safe), cheap, and produces clean extracts and byproducts. The knowledge of the equilibrium phase and the solubility of these compounds in supercritical carbon dioxide, it is of great importance to support the best operating conditions of temperature and pressure for phenolics extraction. The literature reports some solubility values of phenolic compounds in $scCO_2$, such as ferulic acid, coumaric acid, and caffeic acid [19], epicatechin [20], cinnamic acid [21,22], and in $scCO_2$ using ethanol as co solvent of resveratrol [23], quercetin [24] and catechin [25]. Murga et. al. [26] evaluated the solubility of protocatechuic acid, and methyl gallate in supercritical carbon dioxide at temperatures of 40 °C to 60 °C and pressures ranging from 100 to 500 bar. The results showed a crossover pressure of solubility isotherms of about 150 bar and values above 200 bar were well correlated by thermodynamic modeling using the Peng–Robinson equation of state with classic mixing rule.

Considering the importance of solubility data of phenolic compounds in supercritical carbon dioxide, this study aimed to experimentally determine the solubility of protocatechuic acid, chrysin, and sinapic acid by dynamic method at temperatures of 40, 50, and 60 °C, and pressures of 200, 300 and 400 bar, since experimental data only about protocatechuic acid have been reported by Murga et al. [26]. The experimental data were correlated by the Chrastil equation and thermodynamically modeled using the Peng–Robinson equation of state with critical properties and sublimation pressure estimated by grup contribution methods.

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2. Material and methods

2.1. Material and chemicals

Protocatechuic acid (>97%), chrysin (>97%) and sinapic acid (>98%) were purchased from Sigma-Aldrich. Carbon dioxide 99.5% (w/w) (White Martins Gases Industrial, Brazil) was used as a solvent in the process.

2.2. Estimation of critical properties

The critical properties were estimated and the acentric factor was calculated from the molecular structure of the phenolic compounds (Table 1). The density was estimated by the Immirzi and Peinni [27] method. The normal boiling temperature (T_b) was estimated according to the method of Tsibanogiannis et al. [28], which is calculated from the density and molecular weight of the compound. The method proposed by Somayajulu [29] was used to estimate the critical temperature (T_c) and critical pressure (P_c). The acentric factor (ω) was calculated using the Edmister correlation (Eq. (1))

$$\omega = \frac{3}{7}\left(\frac{T_b}{T_c - T_b}\right)\log_{10}\frac{P_b}{P_c} - 1 \quad (1)$$

where P_b = normal boiling pressure (1.0132 bar).

The method proposed by Wlllman and Teja [31] was used to estimate the vapor pressure, which is determined by the boiling temperature as a function of the effective carbon number (ECN), estimating the parameters of the Wagner equation (constant A, B, C and D). Table 2 shows the estimated sublimation pressures.

$$T_b(K) = A_o + A_1(\mathrm{ECN}) + A_2(\mathrm{ECN})^{0.667} + A_3(\mathrm{ECN})^{0.5} + A_4(\mathrm{ECN}) + A_5(\mathrm{ECN})^{0.8} + A_6(\mathrm{ECN})^{0.9} \quad (2)$$

Table 2
Estimated sublimation pressure for the protocatechuic acid, chrysin and sinapic acid.

Compound	ECN	T (°C)	P^{sub} (bar)
Acid protocatechuic	19.889	40	1.706×10^{-9}
		50	6.986×10^{-9}
		60	2.53×10^{-8}
Chrysin	28.866	40	6.18×10^{-18}
		50	9.19×10^{-17}
		60	1.09×10^{-15}
Sinapic acid	25.952	40	2.08×10^{-15}
		50	2.10×10^{-14}
		60	1.75×10^{-13}

$$A = -6.90237 - 0.041529(\mathrm{ECN}) - 0.006503(\mathrm{ECN})^2 \quad (3)$$

$$B = 3.55130 - 0.534943(\mathrm{ECN}) + 0.021867(\mathrm{ECN})^2 \quad (4)$$

$$C = -4.26807 + 0.460198(\mathrm{ECN}) - 0.029179(\mathrm{ECN})^2 \quad (5)$$

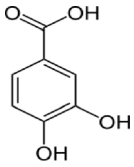
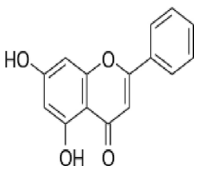
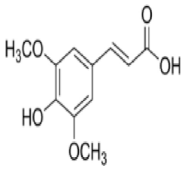
$$D = 5.54103 - 1.93188(\mathrm{ECN}) + 0.029081(\mathrm{ECN})^2 \quad (6)$$

$$\ln\left(P_r^s\right) = \frac{1}{T_R}[A(1-T_R)] + B(1-T_R)^{1.5} + C(1-T_R)^3 + D(1-T_R)^6 \quad (7)$$

2.3. Solubility measurements

The experimental values of solubility of protocatechuic acid, chrysin, and sinapic acid in CO_2 were performed by the dynamic method, whose methodology has been discussed in detail elsewhere [32], in which 1 to 5 g of each acid was placed in a 50 mL extractor containing glass spheres. The extractor was fed with CO_2 to achieve the process conditions of 40 °C, 50 °C, and 60 °C, and 200, 300, and 400 bar. The system was stabilized in static mode for 12 h, and the samples were removed by draining approximately 50 g of

Table 1
Properties of the pure compounds.

Compound	Molecular structure	M_W	Density (kg/m^3)	m_p (K)	T_b (K)	T_c (K)	P_c (bar)	ω
Protocatechuic acid		154.12[a]	1.43[b]	470–473[a] (197–200 °C)	632.27[c] (359.12 °C)	869.29[d] (596.14 °C)	55.33[d]	0.984[e]
Chrysin		254.24[a]	1.34[b]	557–559[a] (284–286 °C)	736.50[c] (463.35 °C)	966.90[d] (693.75 °C)	31.15[d]	1.175[e]
Sinapic acid		224.21[a]	1.33[b]	~475[a] (~202 °C)	706.28[c] (433.13 °C)	927.62[d] (654.47 °C)	28.06[d]	0.973[e]
CO_2	–	44.01	–	–	–	304.1[f] (30.95 °C)	73.75[f]	0.225[f]

[a] Sigma data base.
[b] Estimated by Immirzi and Peinni [27].
[c] Estimated by Tsibanogiannis et al. [28].
[d] Estimated by Somayajulu [29].
[e] Calculated using Edmister correlation (Eq. (1)).
[f] Experimental values reported by Angus et al. [30].