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Measurement and Correlation of 1,4-Naphthoquinone and of Plumbagin Solubilities in Supercritical Carbon Dioxide

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ABSTRACT: The solid solubilities of 1,4-naphthoquinone and of 5-hydroxy-2-methyl-1,4-naphthoquinone (also known as plumbagin) in supercritical carbon dioxide ($scCO_2$) were measured using a static analytical method at 308.2, 318.2, and 328.2 K, and for pressures between 9.1 and 24.3 MPa. For the three studied isotherms, experimental solubilities (in terms of solid molar fraction) ranged from $5.0 \cdot 10^{-5}$ to $4.9 \cdot 10^{-3}$ (for 1,4-naphthoquinone) and from $5.0 \cdot 10^{-5}$ to $9.0 \cdot 10^{-3}$ (for plumbagin). Experimental solubility data were correlated with three density-based models (Chrastil, Bartle, and Méndez-Santiago−Teja models) and with the Peng−Robinson equation-of-state (PR-EOS), together with the conventional van der Waals mixing and combining rules (one adjustable parameter, vdW1; two adjustable parameters, vdW2). Distinct experimental and estimated critical and thermophysical properties of the two solid substances were employed for the PR-EOS correlation and were discussed in terms of the quality of the obtained fitting results. Employed semiempirical density-based models led to AARD values lower than 11 %. Best results were obtained with the Chrastil model: 5.8 % and 8.5 %, for plumbagin and 1,4-naphthoquinone, respectively. Good correlation results were also achieved when using the PR-vdW2 model (with AARD values between 4.0 % and 12.2 %, for both substances and for different isotherms) despite the fact that the adequate choice of the employed critical and thermophysical properties estimation methods was critical for the obtained correlation results.

INTRODUCTION

Chemodiversity in nature offers an unlimited number of natural-based substances with several different and recognized bioactivities.[1] These compounds, usually known as secondary metabolites, are known to provide plant protection against herbivores and pathogenic microorganisms, as well as play an important role in other plant functions, such as structural support (e.g., lignins) or pigmentation (e.g., anthocyanins).[2] Many higher plants can accumulate these extractable organic substances in relatively high quantities to be economically useful and viable as chemical feedstocks or as raw materials for different scientific, technological, and commercial applications, including food, cosmetic, and pharmaceutical ones. Currently, there are a large number of distinct natural-based chemical substances, which have been recognized to present some potentially important pharmacological properties[3], making them desirable candidates for optimization in drug discovery and development processes.[4]

Quinones represent one of the most widespread groups of secondary metabolites in nature. These natural phenolic compounds occur in various families of plants, fungi, bacteria and insects, and play an important role as biologically active compounds in many biological electron-transfer processes, such as respiration and photosynthesis (e.g., vitamin K and coenzyme Q_{10}).[5−8] Plant extracts containing naphthoquinones, an important subgroup of the quinones families, have been used for long time as traditional medicines and, presently, are being the focus of attention of researchers mostly because of their well-known and broad-range of biological activities (such as phytotoxic, insecticidal, antibacterial, fungicidal, anti-inflammatory, antiviral, and cytotoxic effects).[9−14] Moreover, their potential anticarcinogenic and antiamyloidogenic properties make them also potential phytopharmaceuticals for cancer treatment[15] and for neurodegenerative disorders prevention and therapeutics (such as Alzheimer's and Parkinson's diseases).[16]

However, the toxicological and pharmacological effects of most naphthoquinones are strongly dependent on their chemical structures, namely, on the presence and on the molecular position of hydroxyl groups, which can significantly change the physical, chemical, and biological properties of these compounds.[14,17,18] Among all naphthoquinones, plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) is arousing a great interest in recent years because of its effective biological activities such as antioxidant, anti-inflammatory, anticancer, antibacterial, and antifungal effects.[19−25]

The extraction of natural compounds from vegetable raw materials or residues requires the choice of the proper extraction method, as well as the adequate selective and nontoxic solvent, principally if food, cosmetic, and pharmaceutical applications are intended. Moreover, extracts activities and stabilities are also dependent on the employed extraction solvent. The absence of light and of air during the extraction process, together with the use of relatively mild temperatures, are also very important issues as they can significantly reduce extracts degradation.[26]

The increasing necessity of "greener" processes for the extraction of these compounds has recently led to the replacement of some conventional extraction methods (such as maceration or hot extraction using organic solvents), by supercritical fluid (SCF) based technologies, namely, by supercritical carbon dioxide ($scCO_2$) extraction processes. In addition, the possibility of adjusting the supercritical solvent density (by changing process temperature and

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pressure) is one of the advantageous key factors of SCF-based extraction process since it will permit selectivity improvement toward specific compounds. Finally, SCF-based processes are known to reduce or even to avoid the needs for further extracts purification and solvent evaporation steps.

Nevertheless, the design and optimization of extraction and purification SCF-based processes always require an accurate knowledge of the experimental and of the modeled equilibrium solubility data between the solutes of interest and the SCF solvent (at different temperature and pressure conditions).[27] Moreover, other SCF-based technologies, such as SSI (supercritical solvent impregnation/deposition) and rapid expansion of supercritical solutions (RESS) (which can be used in the food and pharmaceutical industry to load bioactive substances, to modify solid particles shape, polymorphism, morphology, and surface structure) are also extremely dependent on the solubility of the pharmaceutical/food ingredient in the SCF solvent.

In this work, the equilibrium solubilities of 1,4-naphthoquinone and of plumbagin in $scCO_2$ were experimentally measured at 308.2, 318.2, and 328.2K, and in a pressure range from 9.1 up to 24.3 MPa. A static analytical method was employed for this purpose. Obtained experimental results were compared with previously reported solubility data for 1,4-naphthoquinone[28−30] and for plumbagin[28] in $scCO_2$, although these were obtained by employing different experimental solubility determination methods or pressure−temperature conditions/ranges. Experimental solubility data were correlated with three density-based models (Chrastil, Bartle, and Méndez-Santiago−Teja models) and with the Peng−Robinson cubic equation-of-state (PR-EOS), together with the conventional van der Waals mixing and combining rules (with one adjustable parameter, vdW1; with two adjustable parameters, vdW2). Different experimental and estimated critical and thermophysical properties of the two solid substances were employed for the PR-EOS correlation procedures and results were discussed in terms of the quality of the obtained fitting results (best average absolute relative deviation values, AARD).

This work continues and extends our previous research activities on the experimental determination and correlation of the solubility of several bioactive substances and of other solid compounds in $scCO_2$,[31−36] as obtained data are critical for the successful design and optimization of supercritical fluid technologies, namely, those to obtain selective naphthoquinones-rich extracts (from different vegetable raw materials sources); those to process the obtained extracts (e.g., micronization and to increase in vivo bioavailability); and those to allow their impregnation/deposition into solid matrices intended for controlled delivery (e.g., for cosmetic and pharmaceutical applications). In all the above-mentioned processes, and in particular in the case of micronization (like RESS) and impregnation processes, the solubility of the solute in the pressurized media (at different conditions of pressure, temperature, and pre/post expansion rates) is one of the main variables affecting the effectiveness of these processes.

EXPERIMENTAL SECTION

Materials. Carbon dioxide (CAS 124-38-9, purity >99.998 % v/v) and ethanol (CAS 64-17-5, purity >99.5 % v/v) were obtained from Praxair and from Panreac Química SA, respectively. 1,4-naphthoquinone (CAS 130-15-4, purity ≥97 % w/w) and plumbagin (CAS 481-42-5, purity ≥95 % w/w) were obtained from Sigma-Aldrich, and were used without further purification. The chemical structures of 1,4-naphthoquinone and of plumbagin are shown in Table 2.

Experimental Solubility Measurement Procedures. Experimental equilibrium solubility data were obtained by a static analytical method and using a solubility apparatus already described and validated in previous works.[31−36] The apparatus comprises a high-pressure stainless-steel equilibrium cell (HPC), coupled to a known-volume sampling loop which is connected through a six-port sampling valve (Rheodyne, model 7060) to previously calibrated volumes. These volumes include tubing lines, a glass trap (immersed in ice) and a stainless steel balloon (immersed in a water bath at room temperature). The sealed HPC is loaded with an excess amount (~600 mg) of each solid substance (1,4-naphthoquinone or plumbagin) and a magnetic stirrer. After closing the HPC, it is placed into a thermostatic water bath, equipped with a temperature controller (ThermoHaake, model DC30) that maintains the experimental temperature within ± 0.1 K. The HPC is then pressurized with CO_2 until the desired experimental pressure is achieved at the chosen operational temperature. Pressure is measured by a high-pressure transducer (Setra, model 204, (0 to 34.4 ± 0.04) MPa). After pressure and temperature stabilization, the mixture is continuously stirred for one hour, followed by a stabilization period of 15 min. A sample is then taken from the HPC into the sampling loop through the six-port sampling valve. The dissolved solid is forced to precipitate into the cold glass trap and after expanding the compressed mixture into the trap and the stainless steel balloon (which was previously brought to subatmospheric pressure). The resulting pressure increase in the balloon is measured using a calibrated high precision low-pressure transducer (Setra, model 204, (0 to 0.175 ± $1.9 \cdot 10^{-4}$) MPa). To recover all the sampled solid substances, a cleaning solvent (ethanol) is injected through the sample loop and the expansion lines and recollected in the same cold glass trap. The tubing lines are additionally cleaned/dried with fresh and slightly pressurized CO_2.

Analytical Method. The amount of solid substance (1,4-naphthoquinone or plumbagin), which was solubilized in $scCO_2$, at the employed pressure and temperature conditions, was quantified by spectrophotometric analysis using a UV−vis spectrophotometer (Jasco V-530, Japan) and previously determined calibration curves (in the range $2.5 \cdot 10^{-3}$ mg·mL^{-1} and $50 \cdot 10^{-3}$ mg·mL^{-1}). The solutes that were collected in each sampling step were diluted to a convenient ethanol volume and the absorbance of the resulting solutions was measured at a fixed wavelength of 332 nm or at 420 nm (for 1,4-naphthoquinone and for plumbagin, respectively). The amount of CO_2 in each sampling step was calculated using the Virial EOS (applied to pure CO_2) as previously reported and explained.[31] All the prepared solutions were carefully stored and protected from light to avoid solid substances degradation.

Correlation of Experimental Solubility Data. *Chrastil Model.* The well-known Chrastil model[37] relates the solubility of a solid solute in a SCF with the density of the pure SCF and with the absolute temperature, according to the following expression:

$$\ln S = k \ln \rho + \alpha/T + \beta \quad (1)$$

In eq 1, S (kg·m^{-3}), is the solubility of the solid in the supercritical phase, ρ (kg·m^{-3}), is the density of the pure supercritical fluid, k, is the association number, α, is a constant,

defined as $\Delta H/R$, (where, ΔH, is the sum of the enthalpies of vaporization and solvation of the solute and R is the gas constant) and β, is another constant, which is related to the molecular weights of the solute and solvent. The parameters k, α, and β, are obtained from a multiple linear regression on the obtained experimental solubility data.

Bartle Model. Bartle et al.[38] developed a straightforward semiempirical correlation which relates the solubility of the solid in the SCF with the experimental pressure, P (bar), and the pure SCF density, ρ (kg·m^{-3}), according to eqs 2 and 3:

$$\ln\left(\frac{yP}{P_{ref}}\right) = A + C(\rho - \rho_{ref}) \quad (2)$$

$$A = a_1 + \frac{a_2}{T} \quad (3)$$

In these expressions, P_{ref}, is a standard reference pressure (set equal to 1 bar), ρ_{ref}, is a reference density (considered as 700 kg·m^{-3}), T is the experimental temperature (K), and a_1, a_2, and C are empirical constants, which are determined by fitting the experimental data obtained for each isotherm using eq 2 and 3. Constant C is assumed as temperature-independent and is an average of the values obtained for each isotherm. Its averaged value is employed to recalculate the A constant for each isotherm, which will then be used to calculate a_1 and a_2 using eq 3. The parameter a_2 is related to the solid solute enthalpy of sublimation, $a_2 = -\Delta H_{sub}/R$, where R is the gas constant.

Méndez-Santiago–Teja Model. Méndez-Santiago and Teja[39] developed a linear semiempirical model which describes the solubility of a solid solute as a function of temperature and of pure SCF density:

$$T\ln(yP) = A' + B'\rho + C'T \quad (4)$$

In eq 4, A', B', and C' are pressure- and temperature-independent constants that are obtained by the multiple linear regression of the solubility data. The consistency of the solubility experimental data can be checked by the convergence of all the solubility isotherms into a single straight line.

Peng–Robinson EOS Model. The equilibrium solubility of a solid solute in a high pressure fluid can be calculated by the general expression

$$y_2 = \frac{P_2^{sub}}{P}\frac{1}{\varphi_2^{SCF}}\exp\left[\frac{v_2(P - P_2^{sub})}{RT}\right] \quad (5)$$

In eq 5, P_2^{sub} is the sublimation pressure of the solid solute, v_2 is the molar volume of the solid, and ϕ_2^{SCF} is the fugacity coefficient of the solid in the fluid phase, which account for the nonideality of the high pressure fluid phase and that can be evaluated by an adequate equation-of-state (EOS). This equation is valid only if the solubility of the solvent in the solid solute is negligible, if the solid is incompressible and if the pure solid saturated vapor (at sublimation) behaves like an ideal gas. The fugacity coefficient of the solid in the fluid phase, ϕ_2^{SCF}, can be calculated from the Peng–Robinson cubic equation-of-state (PR-EOS),[40] described by eq 6 and using the classical van der Waals (vdW) mixing/combining rules with one (vdW1) or with two (vdW2) adjustable binary interaction parameters, k_{ij} and l_{ij}, according to eqs 10 and 11

$$P = \frac{RT}{v - b} - \frac{a}{v(v + b) + b(v - b)} \quad (6)$$

Table 1. Experimental Solubilities of 1,4-Naphthoquinone and of Plumbagin in Supercritical Carbon Dioxide

	T	P	ρ^a	y	S
	K	MPa	kg·m^{-3}	·10^3	kg·m^{-3}
1,4-naphtho-quinone	308.2	9.1 ± 0.04	669.25	0.96 ± 0.018	2.31 ± 0.035
		12.4 ± 0.02	774.37	1.80 ± 0.053	5.02 ± 0.148
		15.2 ± 0.01	817.20	2.32 ± 0.031	6.83 ± 0.091
		18.3 ± 0.06	850.56	2.86 ± 0.058	8.76 ± 0.179
		21.2 ± 0.08	875.33	3.21 ± 0.041	10.14 ± 0.124
		24.0 ± 0.05	894.93	3.50 ± 0.071	11.29 ± 0.234
	318.2	9.2 ± 0.01	361.58	0.14 ± 0.012	0.26 ± 0.022
		12.2 ± 0.03	666.47	1.06 ± 0.042	3.60 ± 0.141
		15.1 ± 0.11	743.88	2.01 ± 0.039	7.62 ± 0.127
		18.5 ± 0.02	795.02	3.00 ± 0.026	12.20 ± 0.102
		21.2 ± 0.03	824.58	3.67 ± 0.038	15.48 ± 0.155
		24.2 ± 0.03	851.13	4.26 ± 0.050	18.56 ± 0.221
	328.2	9.2 ± 0.01	267.80	0.05 ± 0.003	0.07 ± 0.004
		12.2 ± 0.02	515.81	0.78 ± 0.038	2.05 ± 0.098
		15.1 ± 0.01	659.13	1.86 ± 0.048	6.28 ± 0.159
		18.5 ± 0.01	725.52	3.11 ± 0.039	11.52 ± 0.142
		21.2 ± 0.02	771.08	4.28 ± 0.071	16.89 ± 0.282
		24.1 ± 0.01	802.32	4.93 ± 0.030	20.26 ± 0.127
plumbagin	308.2	9.1 ± 0.05	670.37	1.25 ± 0.012	3.58 ± 0.049
		12.3 ± 0.05	771.97	2.41 ± 0.058	7.99 ± 0.185
		15.2 ± 0.01	816.59	3.12 ± 0.108	11.18 ± 0.373
		18.0 ± 0.05	848.04	3.80 ± 0.133	13.85 ± 0.494
		21.2 ± 0.08	875.46	4.55 ± 0.121	17.11 ± 0.461
		24.3 ± 0.04	896.47	5.04 ± 0.121	19.43 ± 0.469
	318.2	9.1 ± 0.14	351.62	0.12 ± 0.008	0.21 ± 0.015
		12.1 ± 0.17	662.08	1.82 ± 0.085	6.17 ± 0.289
		15.2 ± 0.49	745.12	3.40 ± 0.025	12.94 ± 0.084
		18.0 ± 0.52	789.42	4.68 ± 0.058	18.90 ± 0.245
		21.2 ± 0.55	824.45	5.98 ± 0.011	25.29 ± 0.06
		23.9 ± 0.29	848.50	6.95 ± 0.087	30.28 ± 0.387
	328.2	9.2 ± 0.02	267.52	0.05 ± 0.006	0.07 ± 0.007
		12.2 ± 0.07	517.51	1.61 ± 0.040	4.25 ± 0.069
		15.0 ± 0.03	652.39	3.66 ± 0.078	12.22 ± 0.276
		18.4 ± 0.02	728.92	5.80 ± 0.059	21.69 ± 0.246
		21.2 ± 0.02	770.69	7.39 ± 0.032	29.26 ± 0.129
		24.0 ± 0.02	801.00	9.00 ± 0.072	37.09 ± 0.297

[a] Data from NIST webbook (http://webbook.nist.gov/chemistry/).

$$a = 0.45724\left(\frac{R^2T_c^2}{P_c}\right)\left\{1 + n\left[1 - \left(\frac{T}{T_c}\right)^{0.5}\right]\right\}^2 \quad (7)$$

$$n = 0.37464 + 1.54226\omega - 0.26992\omega^2 \quad (8)$$

$$b = 0.07780\frac{RT_c}{P_c} \quad (9)$$

$$a = \sum_i \sum_j y_i y_j (a_i a_j)^{0.5}(1 - k_{ij}) \quad (10)$$

$$b = \sum_i \sum_j y_i y_j \left(\frac{b_i + b_j}{2}\right)(1 - l_{ij}) \quad (11)$$

The optimal binary interaction parameters, k_{ij} and l_{ij}, are obtained through the minimization of the average absolute-relative-deviation (AARD) objective function

$$\text{AARD}\ (\%) = \frac{100}{N} \sum_n \frac{|y^{\text{cal}} - y^{\text{exp}}|}{y^{\text{exp}}} \quad (12)$$

In eq 12, N is the number of experimental data points for each isotherm, y^{cal} are the calculated solubilities, and y^{exp} are the experimental solubility data points.

Estimation of Critical and Thermophysical Properties. The critical properties and the sublimation pressure of both solid substances (1,4-naphthoquinone and plumbagin) were estimated by different methods available in literature to verify its influence on the accuracy of the PR-EOS fitting correlation. The critical pressure (P_c) and critical temperature (T_c) of 1,4-naphthoquinone and plumbagin were calculated using three different estimation methods, namely, the Joback,[41] Wilson-Jasperson[41] and a group contribution method recently proposed by Marrero and Gani.[42] The Pitzer's acentric factor was estimated by the Ambrose−Walton corresponding states method[41] and the molar volume of naphthoquinones were estimated using the Fedors group contribution method.[43] 1,4-naphthoquinone and plumbagin sublimation pressures were estimated by the Ambrose−Walton corresponding states method,[41] assuming that both solids can be treated as subcooled liquids.

RESULTS AND DISCUSSION

The equilibrium solubility of 1,4-naphthoquinone and of plumbagin in $scCO_2$ was experimentally measured at 308.2 K, 318.2 K, and 328.2 K, and in the pressure range from 9.1 MPa to 24.3 MPa. Results are presented in Table 1 and are expressed in terms of the studied solid compounds mole fractions, y, as well as in terms of the mass of solid compounds per unit of volume of $scCO_2$ (S, $kg \cdot m^{-3}$). The overall uncertainty of the performed solubility measurements, taking into account the random uncertainties corresponds to a stated measurement detection limit lower than $1.8 \cdot 10^{-6}$ (in terms of solid compounds mole fractions, y).

The obtained solid compounds mole fraction solubilities varied between $5.0 \cdot 10^{-5}$ and $4.9 \cdot 10^{-3}$ (for 1,4-naphthoquinone) and between $5.0 \cdot 10^{-5}$ and $9.0 \cdot 10^{-3}$ (for plumbagin). The relative standard deviations (RSD) for pressure, for solid compounds mole fractions and for mass of solid compounds per unit of volume of $scCO_2$ are also presented in Table 1. Each reported experimental data point is the average of, at least, three replicate measurements that lead to RSD values lower than 10 %. The solid compounds mole fraction solubilities presented RSD values between 0.6 % (T = 328.2 K, P = 24.1 MPa, $y = 4.93 \cdot 10^{-3}$) and 8.5 % (T = 318.2 K, P = 9.2 MPa, $y = 1.42 \cdot 10^{-4}$) for 1,4-napthoquinone and between 0.2 % (T = 318.2 K, P = 21.2 MPa, $y = 5.98 \cdot 10^{-3}$) and 10.9 % (T = 328.2 K, P = 9.2 MPa, $y = 5.20 \cdot 10^{-5}$) for plumbagin. An overall RSD of 2.6 % was obtained for all experimental data points (and for both compounds). As can be observed and as it was expected, the solubilities of 1,4-napthoquinone and of plumbagin were found to increase with pressure for all isotherms. This is due to the enhanced solute−solvent specific interactions that were favored by the reduction of the intermolecular mean distance of the involved molecules. Moreover, the crossover effect (which is usually found for the solubility of organic solids in $scCO_2$) was also observed for both studied solids, with crossover regions located around 18.0 MPa to 19.0 MPa and around 15.0 MPa to 16.0 MPa, for 1,4-naphthoquinone and for plumbagin, respectively. This retrograde solubility behavior results from the opposite effects of temperature on the SCF density and on the sublimation pressure of the solid solutes. At lower pressures, the decrease in the $scCO_2$ density with the increasing temperature is the dominant phenomenon, leading to a decrease of the solvent capacity and of solute solubility. Above the crossover region (the point at which the three isotherms intercept and cross over each other), the effect of temperature on the solute vapor pressure begins to prevail and thus the solute solubility will increase with increasing temperature.

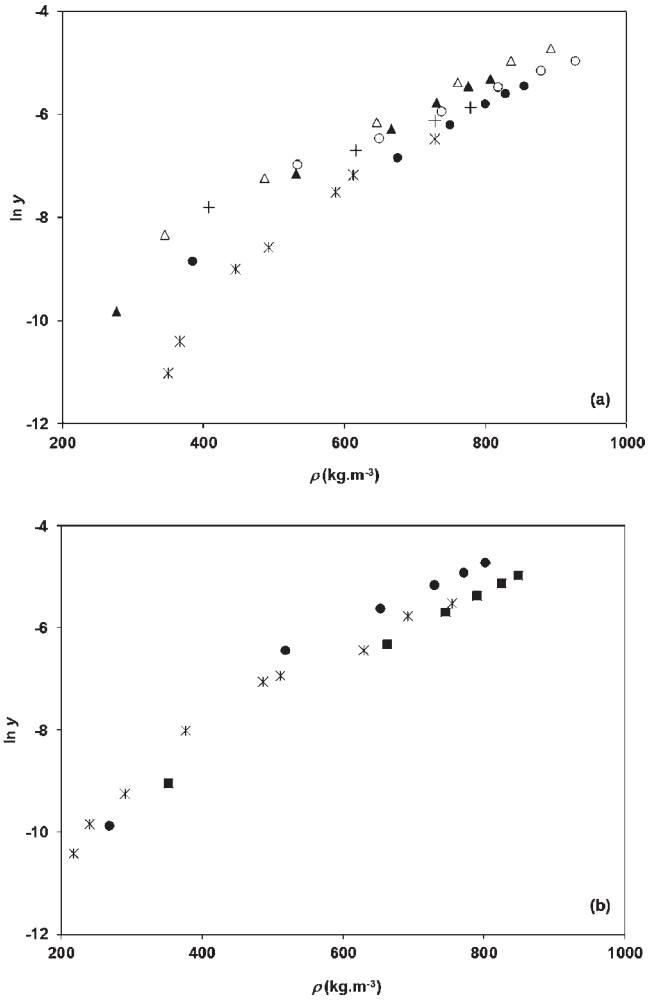


Figure 1. Experimental solubility data in $scCO_2$ of (a) for 1,4-naphthoquinone measured in this work (●, 318.2 K; ▲, 328.2 K) and measured by Schmitt et al.[29] (○, 318.2 K; △, 328.2 K). Data measured at 313.2 K by Ngo et al.[30] (+) and by Rodrigues et al.[28] (∗) are also represented for comparison purposes; (b) for plumbagin measured in this work (■, 308.2 K; ●, 318.2 K) and measured by Rodrigues et al.[28] (∗) at 313.2 K.

The experimental solubilities obtained in this work were compared with other experimental data previously reported in the literature for 1,4-naphthoquinone and for plumbagin (Figure 1).

In the case of 1,4-naphthoquinone (Figure 1a), the experimental data measured by Schmitt et al[29] (at 318.2 and 328.2 K, and using a flow-type apparatus) were always higher than the ones obtained in the present work. The observed differences

were even more pronounced at lower temperatures and pressures and for solid compounds mole fractions lower than $1 \cdot 10^{-3}$. This may be due to larger experimental errors that resulted from the employed analytical procedure (namely, the flow-type method that was used to quantify the amount of solubilized solid and which was based on gravimetric mass differences). Other experimental data (measured by Rodrigues et al.[28] and by Ngo et al.,[30] at 313.2 K and using in situ spectroscopic techniques) are also presented in Figure 2a for comparison purposes. While the results measured by Rodrigues et al.[28] present a pressure-solubility tendency more similar to the one obtained in the present work, the data obtained by Ngo et al.[30] seem to be overestimated.

The only experimental solubility data reported in the literature for plumbagin were those measured at 313.2 K by Rodrigues et al.[28] These values were compared with the ones measured in this work at 308.2 K and 318.2 K (Figure 1b) and seem to be in quite good agreement despite they were measured by different experimental methods.

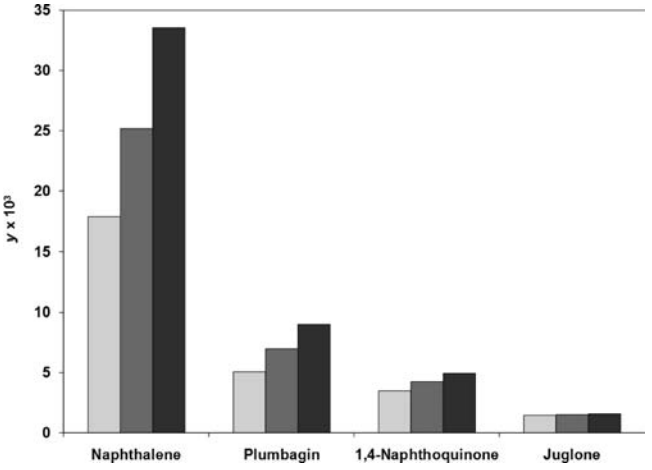


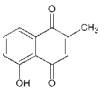
Figure 2. Solubility of naphthalene,[44] 1,4-naphthoquinone (this work), plumbagin (this work), and juglone[36] in $scCO_2$ (at 25 MPa). Results are expressed in terms of solid solute mole fraction at 308.2 K (light gray), 318.2 K (medium gray), and 328.2 K (black).

Generically, 1,4-naphthoquinone can be regarded as a naphthalene derivative since it that can be obtained from its oxidation. This molecule can be then further modified in order to obtain other naphthoquinone derivatives such as plumbagin (5-hydroxy-2-methyl-1,4-naphthoquinone) or as juglone (5-hydroxy-1,4-naphthoquinone). The solubility in $scCO_2$ of all these molecules (naphthalene, 1,4-naphthoquinone, plumbagin, and juglone), expressed as solid solute mole fraction, is compared in Figure 2, for the three different temperatures studied in this

Table 3. Experimental Solubility Correlation Results for 1,4-Naphthoquinone and Plumbagin, Obtained with the Three Density-Based Models (Chrastil, Bartle, and Méndez-Santiago−Teja)

	1,4-naphthoquinone	plumbagin
	Chrastil model	
k	5.05	5.64
α (K)	−5653.11	−6814.25
β	−13.53	−13.30
ΔH (kJ·mol^{-1})	−47.0	−56.7
AARD (%)	8.5	5.8
N	18	18
	Bartle model	
a_1	26.16	32.65
a_2 (K)	−6586.7	−8525.1
C (m^3·kg^{-1})	0.0097	0.010
ΔH_{sub} (kJ·mol^{-1})	54.8	70.9
AARD (%)	10.1	10.5
N	18	18
	Méndez-Santiago−Teja model	
A' (K)	−8853.9	−11201.1
B' (K·m^3·kg^{-1})	3.1	3.4
C'	19.5	26.6
AARD (%)	10.8	10.3
N	18	18

Table 2. Physicochemical Properties of Naphthalene, 1,4-Naphthoquinone, Juglone, and Plumbagin

Solute	Structure	M_w (g.mol^{-1})	V_m (cm^3.mol^{-1})[a]	P^{sub} (Pa)[b] 308.2 K	318.2 K	328.2 K
Naphthalene		128.17	118.0	28.70	69.77	159.03
1,4-Naphthoquinone		158.15	114.8	0.23	0.69	1.96
Juglone		174.15	105.8	0.23	0.53	1.15
Plumbagin		188.18	120.3	0.48	1.03	2.13

[a] Molar volume (V_m) estimated by the Fedors method.[43] [b] Experimental sublimation pressure (P^{sub}) data from Fowler et al.[45] (for naphthalene), and from Kruif et al.[46] (for 1,4-naphthoquinone) and estimated data by the Ambrose−Walton corresponding states method[41] (for juglone and for plumbagin).

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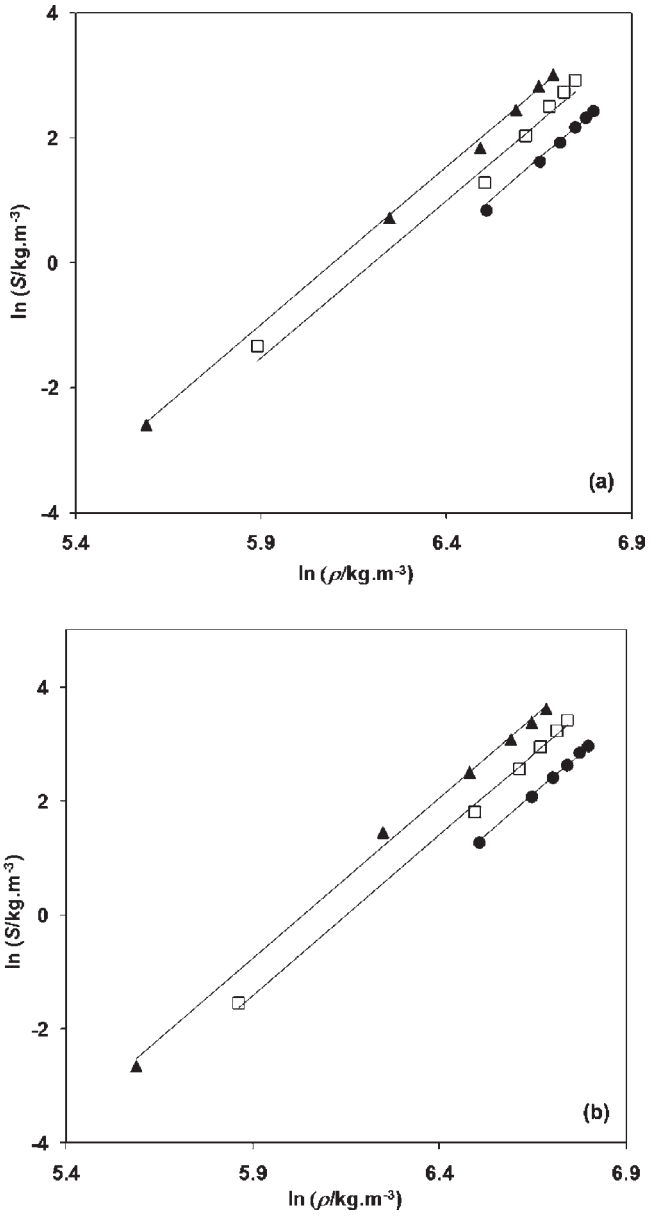

Figure 3. Logarithmic relationship between the solubility of (a) 1,4-naphthoquinone and of (b) plumbagin in $scCO_2$ (S, kg·m^{-3}) and the density of the pure $scCO_2$ (ρ, kg·m^{-3}). Experimental: ●, 308.2 K; □, 318.2 K; ▲, 328.2 K; —, correlated by the Chrastil model (eq 1).

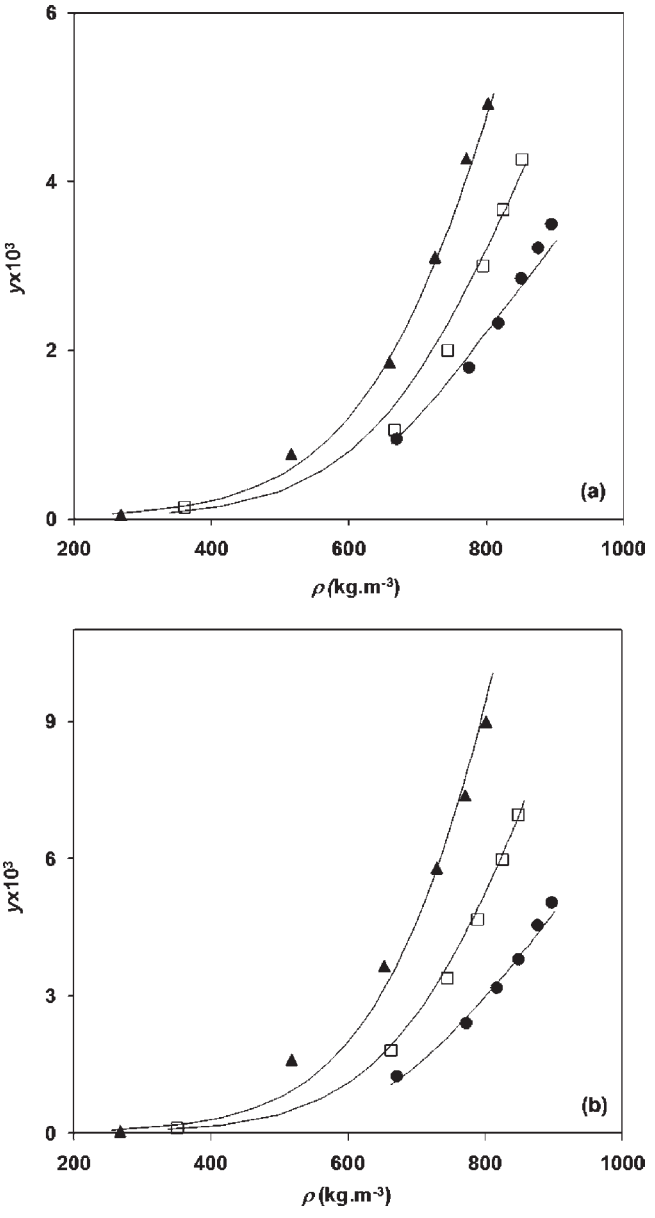

Figure 4. Solubility of (a) 1,4-naphthoquinone and of (b) plumbagin as a function of pure $scCO_2$ density (ρ, kg·m^{-3}). Experimental: ●, 308.2 K; □, 318.2 K; ▲, 328.2 K; —, correlated by the Bartle model (eqs 2 and 3).

work (308.2 K, 318.2 K, and 328.2 K) and at the same pressure (25.0 MPa).

The experimental solubilities of these molecules follow the trend: naphthalene ≫ plumbagin >1,4-naphthoquinone > juglone. As can be verified, the solubility of 1,4-naphthoquinone and of its derivatives is significantly lower than that of naphthalene, decreasing by 3.5 times at 308.2 K and 21 times at 328.2 K, being the lowest solubility observed for juglone. These observed differences can be explained by the less favorable interactions that could be established between naphthoquinones and $scCO_2$, when compared to naphthalene. This is mostly due to the presence of polar groups (hydroxyl and carbonyl) in their chemical structures (and in opposition to naphthalene, which is an apolar molecule). A comparison between the three naphthoquinones shows that (i) when the hydroxyl group is "added" to the 1,4-naphthoquinone molecule (forming juglone), the solubility in $scCO_2$ decreases because of the unfavorable hydroxyl/CO_2 interactions and (ii) when the methyl group is "added" to the juglone molecule (forming plumbagin), the solubility increases 3.5 and 5.7 times at 308.2 K and 328.2 K, respectively, and plumbagin becomes even more soluble in $scCO_2$ than 1,4-naphthoquinone because of the favorable methyl/CO_2 interactions. This means that the low polarity methyl group contribution for the solubility overcomes the high polarity hydroxyl group unfavorable contribution. Additionally, this solubility trend seems not to be directly related with the molecular weight of these substances as well as with their estimated solid molar volumes (Table 2).

However, and above the crossover point, the observed experimental solubilities of these substances follow the same trend as their sublimation pressures (for the three isotherms): as sublimation pressure increases, the corresponding solubilities will

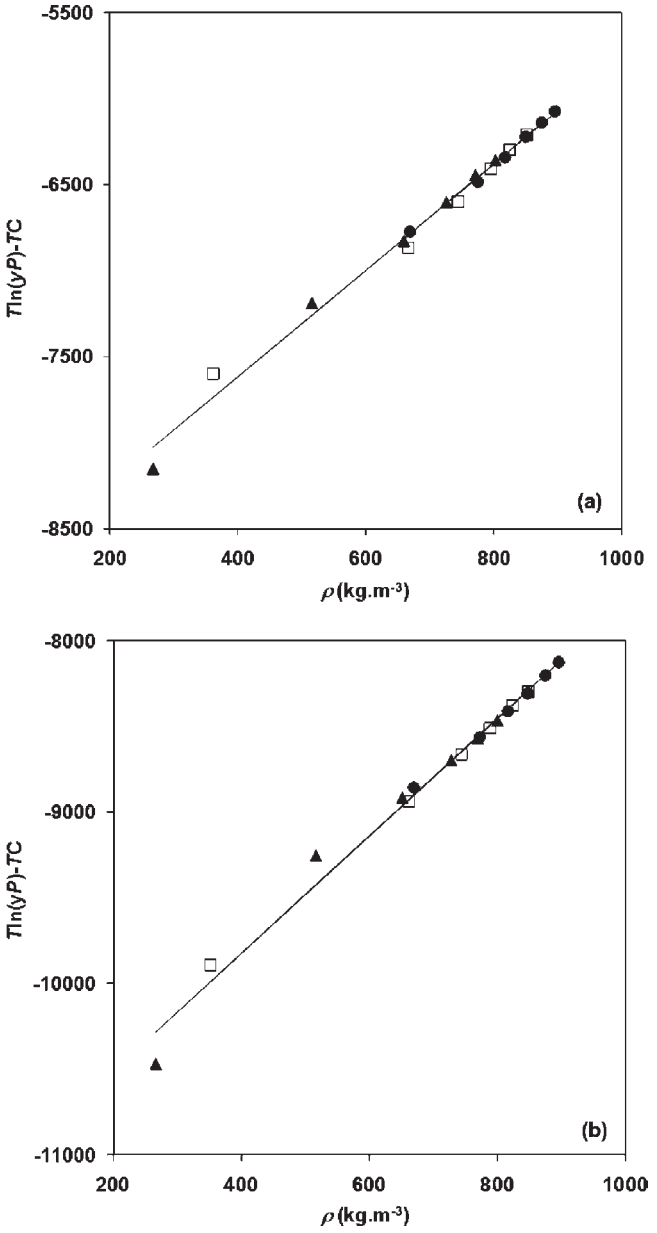

Figure 5. Relationship between the solubility of (a) 1,4-naphthoquinone and of (b) plumbagin and the density of pure CO_2. Experimental: ●, 308.2 K; ■, 318.2 K; ▲, 328.2 K; —, correlated by the Méndez-Santiago−Teja model (eq 4).

also increase. It is also clear that naphthalene and plumbagin present much higher sublimation pressures than 1,4-naphthoquinone and juglone. This is a clear evidence that the solid sublimation pressure is a key factor in the solubilization of these solids into $scCO_2$. Finally, it was also observed that the pressure at which the crossover point occurs increases when solubility decreases, according to the following sequence: naphthalene (12 ± 2 MPa) < plumbagin (15 ± 1 MPa) < 1,4-naphthoquinone (18 ± 1 MPa) < juglone (21 ± 1 MPa).[36,44]

The correlation of experimental solubility data was performed using three density-based correlations (Chrastil, Bartle, and Méndez-Santiago−Teja) and a cubic EOS model (Peng−Robinson EOS with classical van der Waals mixing and combining rules, vdW1 and vdW2). The correlation results and the corresponding AARD values obtained with the three density-based models are shown in Table 3 and represented in Figures 3 to 5.

Results show that the three employed density-based models successfully correlated the experimental 1,4-naphthoquinone and plumbagin solubilities in $scCO_2$, for all experimental isotherms and in the pressure range between 9.1 and 24.3 MPa. Good AARD correlation results were obtained for both solid substances (between 5.8 % and 10.8 %), even at lower pressure/density, which usually present the larger deviations for the fitted curves.

The experimental solubility data were also correlated using the PR-EOS with the vdW mixing and combining rules with one adjustable parameter (PR-vdW1, k_{ij}, $l_{ij} = 0$), or with the vdW mixing and combining rules with two adjustable parameter (PR-vdW2, k_{ij}, l_{ij}). The required critical and thermophysical properties (boiling temperature, acentric factor, solid molar volume, and sublimation pressure) were predicted by different group-contribution estimation methods available in literature, as no experimental data was found with the exception of the experimental sublimation pressure of 1,4-naphthoquinone. Because of their simplicity, these predictive methods are not always reliable and our recent works demonstrated that the choice of the right combination of properties has an important effect on the accuracy of the EOS correlation results.[49−54] In this work and taking in consideration our previous works, this issue was accounted by testing different estimation methods that led to three different sets of estimated properties for 1,4-naphthoquinone (sets 1 to 3) and to two different sets for plumbagin (sets 4 to 5) as presented in Table 4.

In these sets, the solids critical properties were estimated by different methods being the Pitzer's acentric factor and the sublimation pressure estimated by the Ambrose−Walton method,[41] in all cases. The solid molar volumes for 1,4-naphthoquinone and for plumbagin were estimated by the Fedors group contribution method[43] (already presented in Table 2). The influence of the estimation methods on the solid properties is well demonstrated by the large discrepancies observed mainly for the acentric factor and for the solid sublimation pressures which, consequently, will affect the PR-EOS correlation results. For example and in the case of 1,4-naphthoquinone, the influence of the estimated critical properties on the PR-EOS correlation results quality can be assessed by comparing the results obtained by employing set 1 with set 2 of properties, as both used the Ambrose−Walton method to estimate the solid sublimation pressure, while the influence of the sublimation pressure data can be assessed by comparing those results obtained using set 1 with set 3 of properties, as both used the same method for the estimation of critical properties (Marrero−Gani method). The optimal fitted binary parameters as well as the corresponding AARD values, obtained by experimental data correlation using the PR-EOS, are presented in Table 5.

For 1,4-naphthoquinone, reasonable correlation results were obtained when employing the PR-vdW1 and using set 1 (4.6 % to 9.9 % AARD) or set 3 (8.7 % to 12.9 % AARD) of estimated properties. Finally, in general terms and as expected, lower AARD values were observed when the correlation was performed using two adjustable parameters (PR-vdW2). In this case, set 1 (4.0 % to 9.8 % AARD) and set 3 (6.1 % to 9.5 % AARD) of estimated properties led again to good correlation results.

Previous works reported the use of modified versions of the PR-EOS to correlate the experimental solubility data of 1,4-naphthoquinone (for temperatures between 318.2 K and 343.2 K, and for pressures between 10 MPa and 36.5 MPa).[29,48] Despite that the authors observed an improvement in their correlation

Table 4. Estimated Critical and Other Required Thermophysical Properties of 1,4-Naphthoquinone and of Plumbagin[a]

	estimation method				T_c	P_c	T_b		P^{sub} (Pa)		
set	T_c, P_c	T_b	ω	P^{sub}	K	MPa	K	ω	308.2 K	318.2 K	328.2 K
					1,4-naphthoquinone						
1	M-G	M-G	A-W	A-W	871.2	4.290	579.60	0.379	$6.26 \cdot 10^{-1}$	$1.52 \cdot 10^{0}$	$3.49 \cdot 10^{0}$
2	Job	Job	A-W	A-W	877.2	4.070	610.30	0.570	$2.22 \cdot 10^{-2}$	$6.88 \cdot 10^{-2}$	$1.91 \cdot 10^{-1}$
3	M-G	M-G	A-W	Exp.	871.2	4.290	579.60	0.379	$2.26 \cdot 10^{-1}$	$6.89 \cdot 10^{-1}$	$1.96 \cdot 10^{0}$
					plumbagin						
4	M-G	M-G	A-W	A-W	872.4	3.608	610.90	0.554	$3.25 \cdot 10^{-2}$	$9.50 \cdot 10^{-2}$	$2.57 \cdot 10^{-1}$
5	W-J	Pred.	A-W	A-W	1073.8	4.320	657.10	0.100	$4.75 \cdot 10^{-1}$	$1.03 \cdot 10^{0}$	$2.13 \cdot 10^{0}$

[a] M-G: Marrero−Gani method.[42] A-W: Ambrose−Walton corresponding states method.[41] Job: Joback method.[41] Exp: Experimental.[46] W-J: Wilson−Jasperson method.[41] Pred: Predicted by ACD/Labs.[47]

Table 5. PR-EOS Correlation Results for the Solubility of 1,4-Naphthoquinone and of Plumbagin in $scCO_2$, at 308.2 K, 318.2 K, and 328.2 K, Obtained for Different Sets of Critical and Thermophysical Properties

			PR-vdW1		PR-vdW2		
	T	set	k_{12}	AARD	k_{12}	l_{12}	AARD
	K			%			%
1,4-naphtho-	308.2	1	0.114	6.5	0.093	−0.050	4.0
quinone		3	0.067	12.9	0.046	−0.050	9.5
		2	0.048	24.5	−0.084	−0.331	8.1
	318.2	1	0.110	4.6	0.130	0.050	4.2
		2	0.044	27.3	−0.078	−0.304	13.4
		3	0.069	8.7	0.052	−0.041	6.1
	328.2	1	0.100	9.9	0.103	0.007	9.6
		2	0.030	35.7	−0.116	−0.366	15.7
		3	0.065	8.8	0.053	−0.036	6.9
plumbagin	308.2	4	0.062	17.5	−0.005	−0.133	9.0
		5	0.117	5.9	0.151	0.078	5.1
	318.2	4	0.051	23.5	−0.012	−0.140	11.6
		5	0.103	9.0	0.120	0.040	5.2
	328.2	4	0.037	34.9	−0.029	−0151	22.2
		5	0.089	20.8	0.098	0.026	12.2

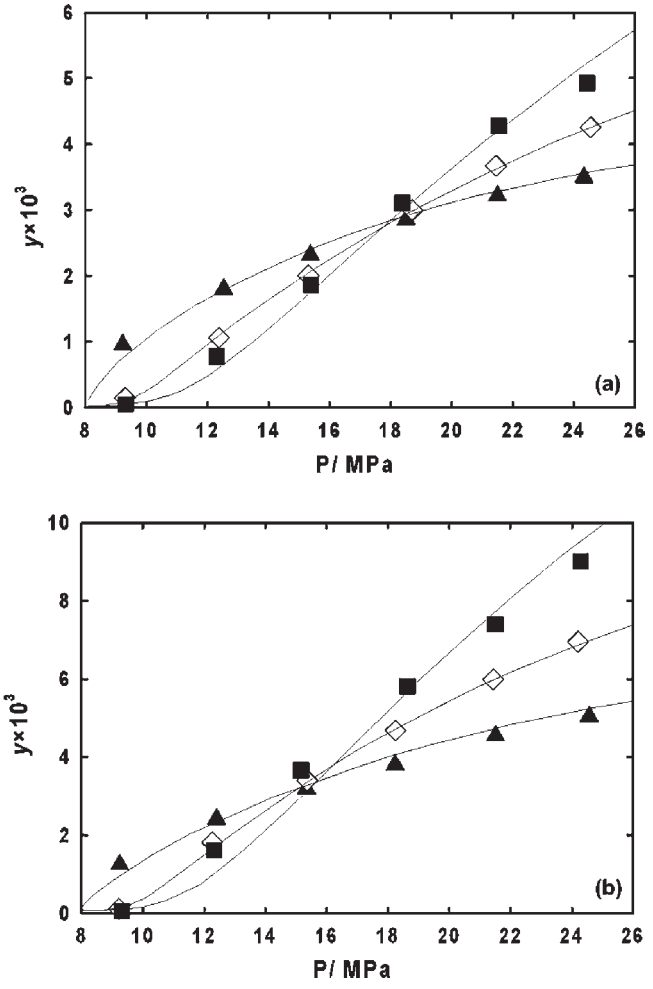

Figure 6. Solubility of (a) 1,4-naphthoquinone and of (b) plumbagin in $scCO_2$. Experimental: ▲, 308.2 K; ◇, 318.2 K; ■, 328.2 K; —, correlated with the PR-EOS model and with the vdW mixing and combining rules. (a) PR-vdW2 model using set 1 of estimated properties (for 1,4-naphthoquinone) and (b) PR-vdW2 using set 5 of estimated properties (for plumbagin). See Tables 4 and 5 for more details.

results (when comparing to the original PR-EOS), they still obtained AARD values of 29 % and 16 % for the vdW1 and vdW2 mixing and combing rules, respectively, which are clearly higher than the ones obtained in the present work. This probably occurred because of the different (and inaccurate) critical and thermophysical properties that were employed in those works. Other models that were attempted to correlate the solubility of 1,4-naphthoquinone in $scCO_2$ included: a simplified cluster solvation model with three adjustable parameters (AARD values of 8.37 %),[49] a modified activity coefficient model coupled with the Flory−Huggins equation with three and four adjustable parameters (AARD values of 13.43 % and 5.31 %, respectively)[50] and a regular solution model with the Flory−Huggins equation with one or two adjustable parameters (AARD values of 21.7 % and 12.7 %, respectively).[51] These literature 1,4-naphthoquinone solubility correlation results (which were obtained by the same PR-EOS model or by other models, using two or more than two adjustable parameters), also confirmed the good PR-EOS data correlation that were obtained in the present work since lower or similar deviations were achieved.

For plumbagin, the PR-EOS correlation results showed that, when employing the PR-vdW1 correlation procedure, set 5 of

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estimated properties was capable to generate good correlations to experimental data (AARD values <10 %) except in the case of the highest temperature (328.2 K) for which an AARD value of 20.8 % was obtained. Set 4 of estimated properties did not lead to good PR-vdW1 correlation results (AARD values between 17.5 % and 34.9 %). However, a significant improvement was observed when experimental data were correlated with two adjustable parameters (using the PR-vdW2 model): once again, set 5 of estimated properties led to the best correlation results for all isotherms (with AARD values between 5.1 % and 12.2 %). The PR-vdW2 correlation results that were obtained using those sets of properties that led to the better correlation results (set 1 for 1,4-naphthoquinone and set 5 for plumbagin) are presented in Figure 6 (for all isotherms).

As can be seen and using these sets of properties, this model is able to accurately describe the pressure dependence of the solubility data for all isotherms as well as the already referred retrograde solubility behavior.

CONCLUSIONS

The solid solubilities of 1,4-naphthoquinone and of plumbagin in $scCO_2$ were experimentally measured using a static analytical method at 308.2 K, 318.2 K, and 328.2 K, and for pressures between 9.1 and 24.3 MPa. Experimental solubility data were correlated with three density-based models (Chrastil, Bartle and Méndez-Santiago−Teja models) and with the PR-EOS together with the conventional van der Waals mixing and combining rules (one adjustable parameter, vdW1; two adjustable parameters, vdW2). Different experimental and estimated critical and thermophysical properties of the two solid compounds were employed for the PR-EOS correlation and were discussed in terms of the quality of the obtained fitting results.

Employed semiempirical density-based models led to AARD values lower than 11 % (for both solid compounds). Best results were obtained with the Chrastil model: 5.8 % and 8.5 %, for plumbagin and 1,4-naphthoquinone, respectively. Good correlation results were also achieved when using the PR-vdW2 model (with AARD values between 4.0 % and 12.2 % for both substances and for different isotherms), despite the fact that the adequate choice of the employed critical and thermophysical properties estimation methods was critical for the obtained PR-EOS correlation results.

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