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Solubility of Azelaic Acid in Supercritical Carbon Dioxide

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In this study, the solubility of azelaic acid in supercritical carbon dioxide has been measured at 313.15 K and 333.15 K over a pressure range of 10 MPa to 30 MPa. A flow-type, dynamic apparatus was used, and the solubility was obtained gravimetrically. The solubility ranged from an azelaic acid mole fraction of $0.42 \cdot 10^{-6}$ (333.15 K, 10.0 MPa) to $10.12 \cdot 10^{-6}$ (333.15 K, 26.7 MPa). The solubility results showed that the crossover point occurred at a pressure between 17 MPa and 20 MPa; at pressures below the crossover pressure, the solubility decreased with increasing temperatures, whereas the opposite was observed beyond the crossover pressure. No solubility data for azelaic acid in any supercritical fluids were found in the literature; thus, there was no reference to compare these results. Two model types were used to correlate the data: density-based models and an equation-of-state (EoS) model. The Chrastil and the modified Méndez-Santiago and Teja (density-based) models were used, and excellent fits were obtained. The Peng−Robinson EoS with standard van der Waals mixing rules was used also with excellent results.

Introduction

Fatty acids can be converted to a variety of valuable chemical intermediates. One of the most abundant fatty acids is oleic acid, and it can be oxidized to form several classes of compounds such as epoxides, monoacids, and diacids. Traditionally, a mixture of ozone and oxygen is used as the oxidizing agent to convert oleic acid to azelaic acid (a diacid) and pelargonic acid (a monoacid).[1] The oxidation occurs in multiphase reactors where the transport of the ozone and oxygen to the liquid phase is typically the limiting step in the process. To overcome the interfacial mass-transfer limitations, the reaction could be carried out in a supercritical medium such as carbon dioxide.[2] A key thermophysical variable to know is the solubility of the reactants and reaction products in the supercritical medium. In this study, the solubility of azelaic acid in supercritical carbon dioxide was determined at 313.15 K and 333.15 K over a pressure range of 10 MPa to 30 MPa. Azelaic acid is a solid at these temperatures and pressures.

Azelaic acid can be used to formulate polyurethanes and polyamides, and pelargonic acid can be used to manufacture lacquers and plastics.[3,4] Due to the versatility of diacids such as azelaic acid, new sources and production pathways are being pursued.[5] For example, azelaic acid is also used in medicine for the topical treatment of skin conditions such as *acne rosacea*, a chronic acneiform disorder affecting the skin.[6] In view of this, the results in this paper could be of interest also to the producers of such medication.

Experimental Section

Materials. Azelaic acid ($HOOC(CH_2)_7COOH$, CAS No. 123-99-9) was supplied by Sigma-Aldrich (minimum 99.0 % purity), and methanol (HPLC grade) was obtained from Fisher Scientific. NexAir (Memphis, TN) provided carbon dioxide (99.5 % purity) and nitrogen (ultrahigh purity). The carbon dioxide (CO_2) was further purified by passing it through a 2 μm filter (Valco Instrument Company, Inc., Houston, TX). All other chemicals were used without further purification.

Procedure. A dynamic technique was used to determine azelaic acid solubility in supercritical carbon dioxide (SC-CO_2). Under the dynamic technique, the assumption is made that the solute−solvent system reaches equilibrium as the solvent passes over the solute.[7] Figure 1 provides a schematic of the supercritical-fluid extractor, manufactured by Thar Technologies (model SFE-100, Pittsburgh, PA), used for the solubility experiments. The system is equipped with a Coriolis mass-flow meter, dual-piston pump, backpressure regulator, and cyclone separator.

A portion of 5 g of azelaic acid was suspended in a stainless-steel equilibrium vessel (volume of 100 mL) using layers of glass wool (Fisher Scientific) and 2 mm diameter borosilicate glass beads (Chemglass, Vineland, NJ). The packing helps minimize channeling of the supercritical fluid and prevents entrainment of the solute.[7,8] The equilibrium vessel, equipped with a heating jacket, was allowed to reach the desired operating temperature of the experiment. Before entering the equilibrium vessel, the CO_2 passed through a heat exchanger, which raised the temperature of the solvent to the necessary value. By the time the CO_2 reached the equilibrium cell, it was in a supercritical state (SC-CO_2). The system was maintained at the desired pressure via the backpressure regulator.

Azelaic acid solubility was determined at 313.15 K and 333.15 K and at pressures ranging from 10 MPa to 30 MPa; experiments were performed in triplicates. For each experiment, a total of 0.6 kg of SC-CO_2 was allowed to flow through the equilibrium cell. The mass of liquefied carbon dioxide used was measured with a Coriolis mass flow meter, and a dual-piston pump propelled the CO_2 at a flow rate of 25 $g \cdot min^{-1}$ (0.42 $g \cdot s^{-1}$). To ensure that equilibrium had been achieved, preliminary solubility experiments were performed at several

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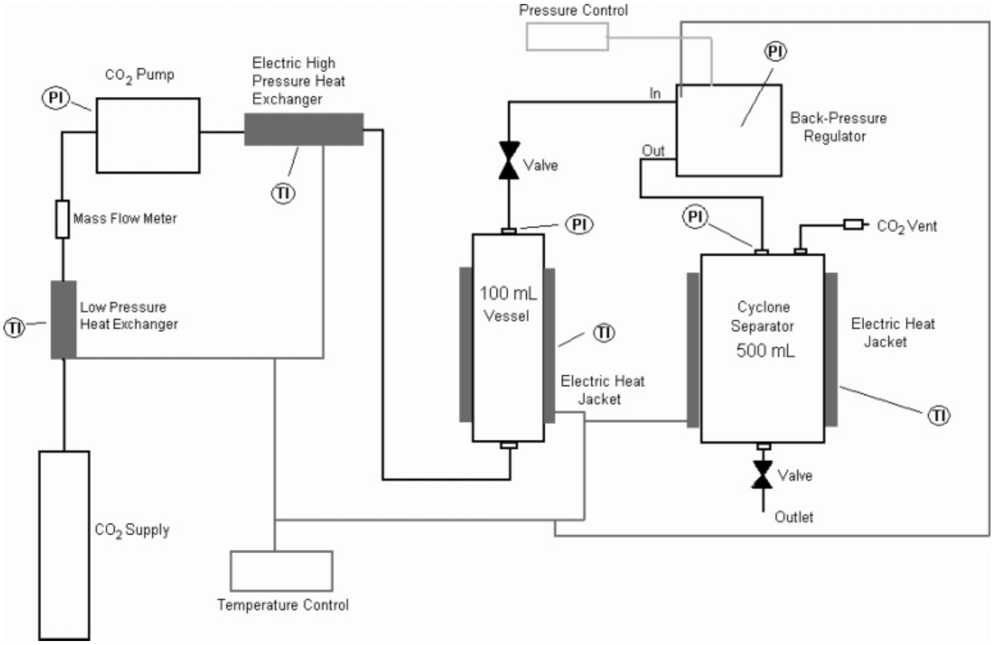

Figure 1. Experimental apparatus.

Table 1. Solubility of Azelaic Acid in Supercritical Carbon Dioxide[a]

T/K	P/MPa	ρ/kg·m^{-3}	average solubility/$10^6 y_2$
313.15	10.0	628.61	1.47 ± 0.09
	13.3	750.23	1.96 ± 0.94
	16.7	803.71	3.44 ± 1.21
	20.0	839.81	1.69 ± 0.61
	23.3	867.59	3.57 ± 2.46
	26.7	890.40	3.33 ± 2.66
	30.0	909.89	7.17 ± 4.19
333.15	10.0	289.95	0.42 ± 0.13
	13.3	525.73	1.72 ± 0.16
	16.7	657.00	2.80 ± 0.17
	20.0	723.68	3.92 ± 0.26
	23.3	768.62	4.84 ± 0.92
	26.7	802.74	10.12 ± 3.89
	30.0	829.71	8.37 ± 0.77

[a] ± uncertainties refer to one standard deviation (σ).

flow rates ranging from 0.33 g·s^{-1} to 0.50 g·s^{-1} at constant pressure. The solubilities determined from these experiments were independent of flow rate. Once the solute/solvent mixture exited the equilibrium cell, it flowed to the cyclone separator where the pressure was reduced; hence, the CO$_2$ became a gas and separated from the azelaic acid. Because azelaic acid is readily soluble in alcohols, a methanol wash of 25 mL was used to dissolve the azelaic acid in the cyclone separator.[9] The azelaic acid/methanol mixture was collected in a tared 40 mL amber glass vial, and then the methanol was removed using a TurboVap model LV (Caliper Life Sciences, Hopkinton, MA), which evaporated the solvent using a stream of nitrogen. Once the methanol was removed, the vial was weighed with a balance (Mettler Toledo model AB265-S/FACT, Columbus, OH) to determine the mass of azelaic acid collected from the experiment. Between experiments, the equilibrium vessel was taken offline, and SC-CO$_2$ was used to clean the tubing of the experimental apparatus.

Results and Discussion

The solubility results of azelaic acid in SC-CO$_2$ are summarized in Table 1. The density of CO$_2$ was obtained from the NIST fluid property database.[10] In general, as pressure was elevated at constant temperature, the solubility of azelaic acid in SC-CO$_2$ increased. At lower pressures, the solubility at 333.15 K is lower than the solubility at 313.15 K. However, the crossover pressure occurs between 16.7 MPa and 20.0 MPa, and from that point forward, solubility was higher at 333.15 K than at 313.15 K. This indicated that the vapor pressure of azelaic acid began to have a dominant effect on solubility.

Modeling is often used to correlate solubility data. Two approaches are generally found in the literature: the so-called semiempirical methods, many of which derived from the one originally proposed by Chrastil,[11] and the equation-of-state methods.

Semiempirical Methods. Chrastil developed a theory based on the law of mass action applied to the formation of a solvate complex between a solute molecule and a number of solvent (SCF) molecules.[11] This theory leads to the following equation for the solubility of component 2 (solid or liquid) in component 1 (SCF)

$$c_2 = \rho_1^k \exp\left(\alpha + \frac{\beta}{T}\right) \tag{1}$$

so that a log−log graph of c_2 vs ρ_1 for isothermal data should give a straight line. In eq 1, c is the concentration of solute in the supercritical fluid; ρ is the density of the supercritical fluid; k is an association number; α is a function of the molecular weights of the solute and supercritical fluid; β is a function of the heat of solvation and heat of vaporization; and T is temperature. Later, this equation was slightly modified to include a more accurate effect of temperature.[12]

$$c_2 = \rho_1^k \exp\left(\alpha + \frac{\beta}{T} + \frac{\gamma}{T^2}\right) \tag{2}$$

where the γ term offsets variation of the heat of vaporization with temperature and the other variables are the same as previously defined for eq 1.

As shown in Figure 2, a log−log graph of c_2 vs ρ_1 for isothermal data still shows a linear relationship. This plot clearly shows that concentration of azelaic acid in the SC-CO$_2$ increases with increasing density. The values for k, α, and β in eq 1 were determined to be 3.86, −16.27, and −4439.06, respectively, via

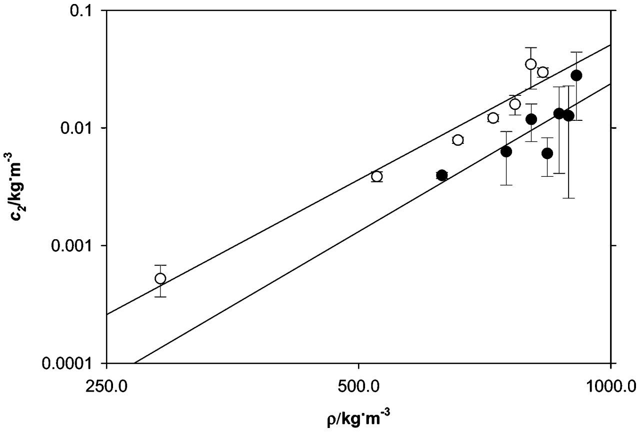

Figure 2. Chrastil plot of azelaic acid solubility in SC-CO$_2$: ●, 313.15 K; ○, 333.15 K; —, Chrastil model prediction.

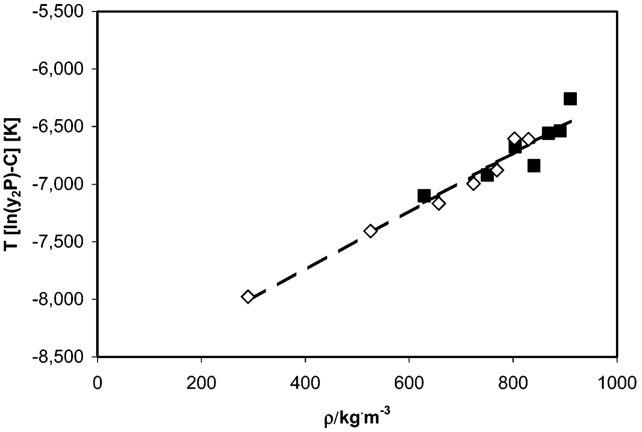

Figure 3. Méndez−Teja plot resulting from multilinear regression of eq 4: ■, 313.15 K; ○, 333.15 K; - - -, model prediction.

multilinear regression using Polymath 5.1 (Polymath Software, Willimantic, CT). For the regression analysis, c and ρ were both expressed in kg·m^{-3}, and T was expressed in K. Also, Figure 2 illustrates that the concentration of azelaic acid is generally higher at 333.15 K than at 313.15 K. The error bars therein correspond to one standard deviation calculated based on the three measurements done at the corresponding temperature and pressure (as mentioned before, each solubility measurement was done in triplicate).

In the above methods, no properties of the solute are required. Other methods have been proposed later by Méndez-Santiago and Teja[13,14] that require the sublimation pressure of the solid, which is not always available. They proposed to plot the so-called enhancement factor as a function of the density of the solvent in the following form

$$T \ln E = T \ln \frac{y_2 P}{P_2^{\text{sub}}} = A + B\rho_1 \tag{3}$$

where T is absolute temperature; E is the enhancement factor; y is the solute mole fraction; P is total pressure; $P_2^{\text{sub}}$is the sublimation pressure of the solute; ρ is the density of the supercritical fluid; and A and B are regressed constants. This should give a straight line. The enhancement factor represents the ratio of the actual solubility to the ideal solubility, i.e., that calculated according to the ideal-gas law (P_2^{sub}/P). The main advantage of this model is that solubility data at different temperatures can be represented by a single straight line.

They also proposed a modified version of the method for cases in which the sublimation pressure was unknown. This is obtained by substituting a two-constant Antoine equation for P_2^{sub} into eq 3

$$T \ln y_2 P = A' + B\rho_1 + CT \tag{4}$$

where A', B, and C are regressed constants. All other variables in eq 4 are the same as those defined in eq 3.

A two-step procedure is needed in this case. First, constants A', B, and C should be determined for a given data set by a regression method; then, a plot of $T(\ln y_2 P - C)$ vs ρ_1 is prepared and should give a straight line. This method (original or modified version) provides an excellent tool to test the consistency of data taken at different temperatures. For this study, eq 4 was used to model the results. The values for A', B, and C were determined to be -8746.98 K, 2.52 K·m^3·kg^{-1}, and 11.54, respectively, via multilinear regression using Polymath 5.1 (Polymath Software, Willimantic, CT). For the regression analysis, P, ρ, and T were expressed in MPa, kg·m^{-3}, and K, respectively. Figure 3 shows that the data points for both isotherms follow a single trend, indicating good consistency of the data over the range of temperatures tested. A variant of the Méndez−Teja approach using reduced variables is presented by Sparks et al.[15] The main advantage of this variant is that the model parameters have no units.

Equation-of-State (EoS) Methods. In this approach, the solubility is obtained from the following phase-equilibrium equation

$$y_2 = \frac{P_2^{\text{sub}}}{\hat{\phi}_2 P} \exp\left(\frac{V_2^{\text{sol}} P}{RT}\right) \tag{5}$$

where the variables in the pre-exponential factor are sublimation pressure of the solid, fugacity coefficient of the solid in the supercritical fluid phase, and total pressure, and those in the exponential argument are molar volume of the solid, universal gas constant, and absolute temperature. This equation comes from an exact thermodynamic equation and is subjected to two standard and fully justified assumptions, both stemming from the fact that sublimation pressures are usually extremely low: (a) $P \gg P_2^{\text{sub}}$, and (b) at T and P_2^{sub}, $f_2^{\text{sub}} \approx P_2^{\text{sub}}$. All variables in eq 5, except $\hat{\phi}_2$, can be readily obtained. Obtaining $\hat{\phi}_2$, however, entails some complexity. Cubic equations of state are normally used to this end, although other types have been used by some authors as recently reviewed in the literature.[16] Some of the difficulties of EoS in general and of cubic EoS in particular are: (a) $\hat{\phi}_2$ is a function of y_2, and thus iteration is required; (b) the critical point of most pure solids of interest is unreachable, and thus, their critical properties are virtual variables (usually they are estimated by group contribution methods); (c) the sublimation pressure of solid solutes normally encountered in supercritical extraction processes is hard to measure and thus has to be also estimated; and (d) the choice of the proper EoS and mixing rules is not trivial given the myriad of choices available nowadays. Item (a) above is rather minor given the increased capacity of computers and computer software; the others remain to be a challenge. In this work, the Peng−Robinson EoS and van der Waals mixing rules, with one binary interaction parameter (in the combination rule for parameter a), have been chosen for modeling purposes. The best interaction parameter was found by minimizing an objective function as defined by Caballero et al.,[17] and they were 0.132 at 313.15 K and 0.165 at 333.15 K. Physical properties of carbon dioxide and azelaic acid used for the EoS calculations are available as Supporting Information. These properties include critical tem-

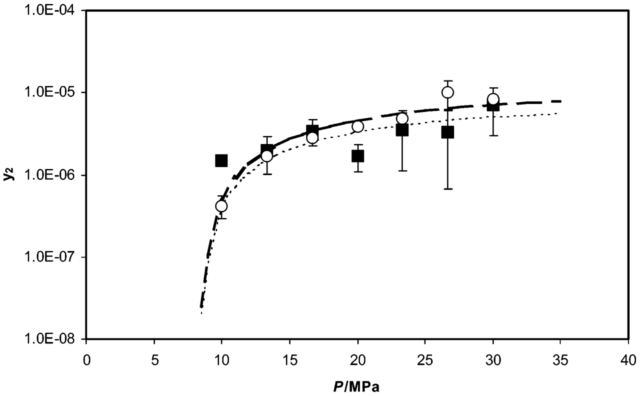

Figure 4. Experimental and EoS-predicted solubilities of azelaic acid in SC-CO_2: ■, 313.15 K; ○, 333.15 K; - - -, 313.15 K EoS prediction; —, 333.15 K EoS prediction.

perature (T_c), critical pressure (P_c), acentric factor (ω), molecular weight (MW), sublimation pressure (P^{sub}), normal boiling point (T_B), and density (ρ). Figure 4 shows how the experimental solubility data compare to those predicted by the Peng−Robinson EoS. (Error bars shown are the same as in Figure 2.) The solubility data at 333.15 K fit the EoS model better than the 313.15 K data. This could be due to the increased variance of the data at 313.15 K. Figure 4 also illustrates that, in general, azelaic acid solubility increased as pressure was increased.

Conclusions

The solubility of azelaic acid in supercritical carbon dioxide has been determined experimentally. To the authors' knowledge, this is the first set of reported data for this system. The solubility varied from an azelaic acid mole fraction of $0.42 \cdot 10^{-6}$ at 333.15 K and 10.0 MPa to $10.12 \cdot 10^{-6}$ at 313.15 K and 26.7 MPa. Due to the low solubility of azelaic acid in SC-CO_2, determining the extracted amount of azelaic acid gravimetrically resulted in large variations in the data (especially the 313.15 K data set). In general, the solubility of azelaic acid increased with increasing temperature only after exceeding the crossover pressure that occurred between 17 MPa and 20 MPa. Both the semiempirical methods and the equation-of-state approach to modeling the data provided good correlations.

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Supporting Information Available:

Physical properties of carbon dioxide and azelaic acid used for EoS calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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