EXPERIMENTAL DETERMINATION AND MODELING OF COUMARIN SOLUBILITY IN SUPERCRITICAL CARBON DIOXIDE

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Abstract. Coumarin and its derivatives are bioactive compounds with great potential for pharmaceutical, cosmetic and food applications. These compounds are present in a great variety of vegetable matrices. Nowadays, one of the ways utilized for their production is supercritical fluid extraction, and thus knowledge on solubilities is very important for process design and optimization. In this work, the solubility of coumarin in supercritical carbon dioxide was measured at isothermal conditions (308.15, 315.15, and 321.15 K) at 10, 12.5, and 15 MPa, using a visual cell and a pseudo-static method. The values of solubility that were determined (in the order of 10^{-4} mole fraction) agree with those measured by Choi *et al.* (1998), but grossly disagree with Rodrigues *et al.* (2008) (in the order of 10^{-2} mole fraction), which might be attributed to the different experimental methodology that was used. Most interesting, above 10 MPa (from 343.05 to 314.15 K) a melting point depression for coumarin was observed. In addition, a crossover region for solubility was evidenced experimentally between 10.8 and 11.8 MPa. The semiempirical model of Chrastil and Foster's deduction appropriately describe the observation for the crossover region, with an average absolute deviation (AARD) equal to 5.12%.

Keywords: solubility, coumarin, melting point, crossover pressure, carbon dioxide.

1. Introduction

Coumarin is a secondary metabolite that is widely distributed in the plant kingdom, particularly in the *Orchidaceae*, *Leguminoceae*, *Rutaceae*, *Umbelliferae*, and *Labiatae* orders [1]. This compound and its derivatives have a wide range of industrial applications, mainly for cosmetic, pharmaceutical and food purposes, due to their antioxidant capacity and also to their different properties and biological functions [2]. Nowadays, their beneficial effects on health are being largely evaluated [2-5] in studies ranging from analgesic properties to applications in cancer treatments [5].

Much of the coumarin available in the world market is produced by organic synthesis [3]. However, the increasing consumer preference for compounds of natural origin has promoted its extraction from vegetable matrices [6]. Thus, the supercritical fluid (SCF) technology is a potential alternative that can be applied to obtain coumarin and its derivatives from natural sources. As it is well known, supercritical carbon dioxide (SC-CO_2) has been used as solvent because it allows one to obtain solvent-free extracts with superior antioxidant activity and organoleptic properties [7]. Furthermore, the attractive physical and toxicological inertness properties of SC-CO_2 have made it an ideal medium for green chemistry processes such as separations, particle micronization, encapsulation, and materials processing [8].

Experimental information on coumarin solubility in SC-CO_2 and its dependence on pressure and temperature are of great importance for designing SCF extraction processes of this substance. This information is required as a first step to improve the overall selectivity and yield [9]. In recent years, some

studies have reported the existence of two interesting phenomena in solute-supercritical solvent systems: crossover pressure and melting point depression [8, 9]. These phenomena occur at high pressures in the presence of a compressed gas. The crossover pressure has been used to design extraction processes for selective separations in multi-solute systems [9], whereas the solute melting point depression has aroused great interest in applications involving chemical synthesis [8].

In this work we present experimental measurements of coumarin solubility in SC-CO_2, and we report for the first time the existence of a melting point depression for coumarin. In addition, we analyze the pressure dependence of melting point, and develop a model based on the Clapeyron equation for predicting the melting temperature of coumarin in the presence of SC-CO_2. Finally, the accuracy of the Chrastil model and the Foster deduction to predict the crossover pressure region were evaluated.

2. Experimental

2.1. Materials

Carbon dioxide (99.9%) was supplied by Oxígenos de Colombia S.A (Cali, Colombia). Coumarin-1 (synthesis grade) and ethanol (99.9%) were purchased from Merck (Colombia). All these chemicals were used without further purification.

2.2. Experimental apparatus and procedure

Figure 1 shows a schematic representation of the experimental apparatus that was used for determining the solubility of coumarin in supercritical carbon dioxide. This apparatus was designed and built in the High Pressure Laboratory at Universidad del Valle, Colombia [10], but it was adapted in this work for quantitative sampling in solubility measurements. Experimental measurements of solubility were performed following a procedure similar to that described by Dohrn [11]. In a typical solubility experiment, 12 g of coumarin were loaded into a 250 cm^3 visual cell. Then, the cell was placed inside an isothermal air bath and was equilibrated at the desired temperature (308.15, 315.15 and 321.15 K). Temperature in the isothermal bath was controlled by using a K-type thermocouple that was located inside an aluminum block, and was connected to a PID controller. The temperature inside the cell was independently determined by using a J-type thermocouple connected to a digital thermometer (Fluke, model 52-2). A pneumatic pump (Williams-Milton Roy, model CP250V225) was used to load CO_2 into the cell to approach the working pressure (10 MPa, 12.5 MPa and 15 MPa), and a manual pump (HiP, model 62-2-10) was then used to finely adjust the desired pressure. The pressure inside the cell was determined with a Bourdon pressure gage (Heise, model AISI 403, 12 inch diameter, 0-7500 psi, with 10 psi divisions). The dissolution of coumarin in CO_2 inside the cell was visually monitored using a video system. The mixture was magnetically stirred during 30 min to reach equilibrium. An excess of pure solid coumarine was observed in the cell in all the experiments.
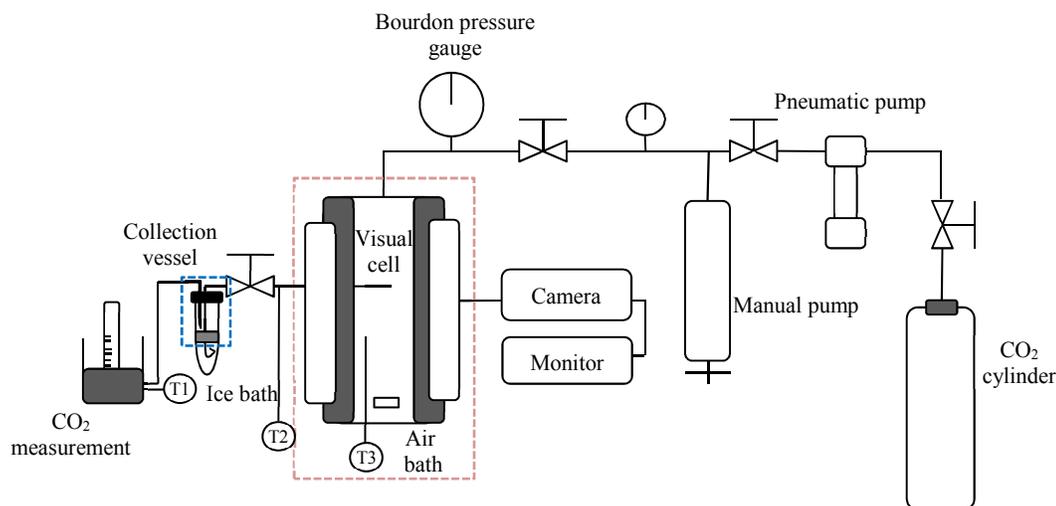

Figure 1. Experimental apparatus for solubility measurements

When the mixture coumarin-CO_2 was in equilibrium a small sample of the CO_2 phase was taken through a 1/16" line located on the upper part of the cell. This line was heated to avoid obstructions during sampling due to a possible precipitation of coumarin, heating of the sampling line was performed by using a 60 W resistance connected to a variac. The temperature of the sampling line was independently determined using a K-type thermocouple connected to a digital thermometer. The thermocouples were calibrated against a precision RTD (Fluke, model 1512A) whose calibration is in turn traceable to a NIST standard. Temperatures are believed to be accurate to ± 0.3 K. The pressure gage was calibrated against a dead weight meter. Pressures are then accurate to ± 5 psi.

The sample was collected in a test tube submerged into a salt-ice bath at -10 °C. The end of the sampling line inside the tube was surrounded by a cotton filter that acts as a solute trap and eliminates the loss of coumarin during sample collection. In all cases, from five to eight consecutive samples were taken to check for reproducibility.

2.3. Analytical method

The amount of CO_2 in each sample was quantified by determining the volume of water displaced by this gas after decompression. Provisions were taken to take into account the vapor pressure and temperature of the displaced water. To determine the amount of coumarin in each sample, the collected solid sample was diluted in 5 cm^3 of ethanol. The resulting solution was analyzed by UV spectrometry in a UV-VIS spectrophotometer (Thermo Scientific, model Evolution 60) at 282 nm. The calibration of this instrument was made using five standard samples with concentrations from 2.5 to 20 mg/L. A linear equation was applied to correlate concentration with absorbance (R^2=0.9985). Finally, the solubility of coumarin in supercritical carbon dioxide was calculated by the equation:

$$y = \frac{n_{cou}}{n_{co_2} + n_{cou}} \qquad (1)$$

where y is the solubility of coumarin in mole fraction, n_{cou} is the amount of coumarin in the sample as determined through the analytical method, and n_{co_2} is the amount of carbon dioxide in the sample that was measured by using the described volumetric method. Finally, a statistical analysis was developed in order to variation coefficient minimization.

3. Results and discussion

3.1. Solubility of coumarin

The solubility of coumarin in supercritical carbon dioxide was measured at 308.15, 315.15 and 321.15 K, at pressures between 10 and 15 MPa (see Figure 2 and Table 1). The values in Table 1 correspond to averages of 5 and 8 samples. Variances of the data are indicated in Figure 2 by error bars. The obtained values are in the same order of magnitude (~10^{-4} mole fraction) to those reported by Choi *et al.* [14], but differ from those reported by Rodrigues *et al.* [15] by two orders of magnitude. These differences might be attributed to the different methodologies that were used in the three studies.

Graphical representation of the data indicates the presence of a crossover point between 10.8 to 11.8 MPa. In fact, below 10.8 MPa the solubilities follow the order $y_{308,15\,K} > y_{321,15\,K} > y_{315,15\,K}$, and above 11.8 MPa this order reverses. It is interesting to note, however, that at 10.8 MPa the determined solubilities values do not increase monotonically with increasing temperature. This is in contrast with the observations of Foster *et al* [13], in which such monotonic increase was found for several systems at pressures below that of the crossover point. Conceivably, a non-monotonic change of solubility with temperature at constant pressure may be due to a phase transition of the solute (i.e., melting) induced by the presence of the compressed supercritical fluid. Foster *et al.* mentioned such a possibility but in many cases this cannot be verified because many measurements that are reported were obtained using non-visual equilibrium cells. By using a visual cell, in this work we were able to determine a melting point depression for coumarin, as it will be discussed ahead in this paper.
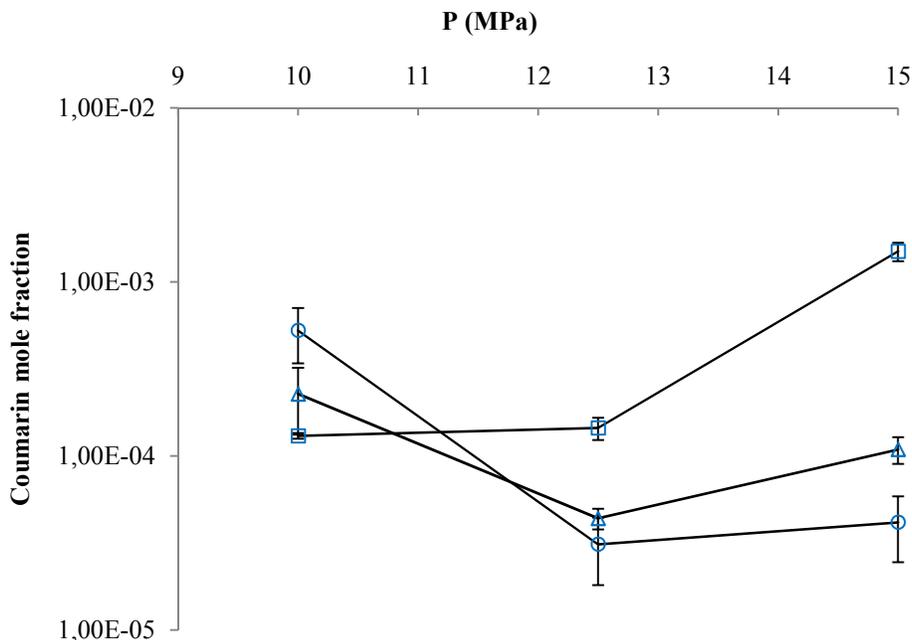
P (MPa)

Figure 2. Solubility of coumarin in supercritical carbon dioxide at (o) 308.15 K, (□) 315.15 K, (Δ) 321.15 K

Table 1. Coumarin solubility in supercritical carbon dioxide

Temperature (K)	Pressure (MPa)	Solubility (mole fraction $x\ 10^4$)
308.15	10.0	5.24 ± 1.84
308.15	12.5	0.31 ± 0.13
308.15	15.0	0.42 ± 0.17
315.15	10.0	1.30 ± 0.05
315.15	12.5	1.45 ± 0.21
315.15	15.0	14.90 ± 1.81
321.15	10.0	2.26 ± 0.94
321.15	12.5	0.44 ± 0.06
321.15	15.0	1.09 ± 0.19

3.2. Semiempirical modeling and crossover pressure

The well-known model by Chrastil [12] was used for modeling the solubility data. This model is expressed by the equation:

$$s_{sol} = \rho_{scs}^k \ exp\left(A + \frac{B}{T}\right) \tag{2}$$

where ρ_{scs} is the density of the pure supercritical solvent (kg/m^3), s_{sol} is the solubility of the solute (kg·m^{-3}), A is a an adjustable parameter that is a function of enthalpies of solvation and evaporation, B is a function of entropies of solvation and evaporation, the association coefficient and the molecular weights of the pure solute and the pure supercritical solvent; and T is temperature (°C). The association parameter k represents the amount of molecules of the solvent that interact with one molecule of solute. We used the Peng Robinson equation of state for determining ρ_{scs}.

For existence of a crossover pressure region it is necessary that all solubility isothermal lines converge at the same region or point. According to Foster *et al.* [13], the criterion for the determination of the crossover pressure region is:

$$\left(\frac{\partial ln(s_{sol})}{\partial T}\right)_P = 0 \tag{3}$$

Deriving Equation 2 and substituting into Equation 3:

$$\left(\frac{\partial \ln(s_{sol})}{\partial T}\right)_P = k\left(\frac{\partial \ln(\rho_{scs})}{\partial T}\right)_P - \frac{A}{T^2} \tag{4}$$

Equation 4 was applied to estimate the pressure crossover range of coumarin. Table 3 shows a comparison of experimental and predicted results. Observe that the semiempirical model of Chrastil and Foster's deduction appropriately describes the observations for the crossover region, with an average absolute deviation (AARD) equal to 5.12%. This in agreement with the previous work by Foster *et al.* [13], in which the AARD for polar and nonpolar compounds varied from 0.2 to 16.8 %. Note that the use of the Chrastil model allows one to reduce the mathematical complexity and the computational effort.

Table 2. Crossover pressure region for coumarin

Determination Form	Pressure range (MPa)	Mean Value (MPa)
Experimental	10.8 – 11.8	11.3 ± 0.5
Predicted using Foster's deduction	10 – 11.5	10.75 ± 0.75

3.3. Melting point depression

In this work, the melting point depression for coumarin was visually observed. In fact, at atmospheric pressure (0.0901 MPa) the melting temperature that was measured for coumarin in our laboratory by the conventional capillary method was in the interval 340.65 to 345.15 K (i.e., the temperature for melting the first crystal and that for the last one). In contrast, at 10.34 MPa in the presence of compressed CO_2 the interval of melting temperature that was observed was 314.15 to 318.15 K.

Melting point depression has been recently reported for different types of compounds such as polymers, lipids, and ionic liquids [16]. In order to model this phenomenon, several approximate approaches have been proposed, mainly based on equations of state [17] and semiempirical models [18]. In addition, Lian *et al.* [19] suggested that this behavior can be described by using the Clapeyron equation. To illustrate, Figure 3 shows the melting point curve for naphtalene in the presence of supercritical carbon dioxide. Note that the equation captures the overall tendency of the data, but it does not make an accurate description of them.

Figure 4 shows the melting point curve for pure coumarin in the presence of supercritical carbon dioxide. Although only two experimental data were determined, that was enough to obtain the Clapeyron constants and make an estimate of the complete melting point curve. The literature has shown that AARD values of up to 39.8% are usually obtained when only two points are used for describing this behavior [20].

Table 2 shows the phases of coumarin in the presence of compressed carbon dioxide in the range of pressures that was studied (10 to 15 MPa) for the solubility measurements. The phases reported were obtained with the Clapeyron equation (i.e., by looking at Figure 4) and are in agreement with the visual observation of phase changes that were made. In fact, at 308.15 K coumarin is solid while at 321.15 K is liquid for the range of pressures that was considered.

Table 3. Phases of pure coumarin in the presence of compressed CO_2 in the range 10 to 15 MPa

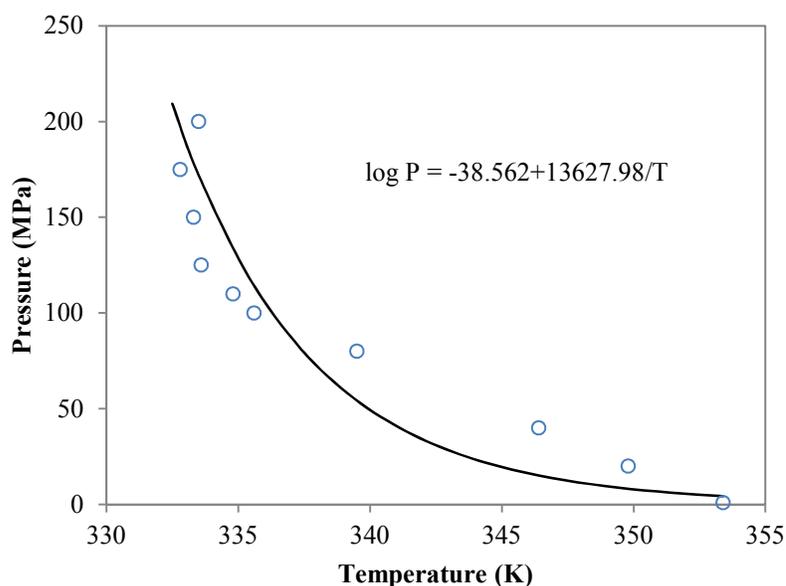| Temperature (K)	Phase
308.15	Solid
315.15	Solid+Liquid
321.15	Liquid

Figure 3. Melting point curve for naphthalene in supercritical carbon dioxide. (o) experimental data and (−) correlation using the Clapeyron equation.
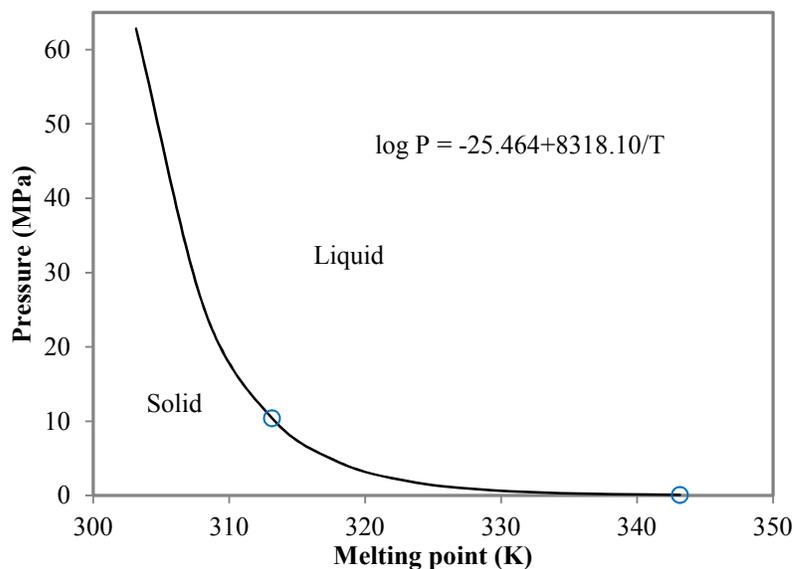

Figure 4. Melting point curve for coumarin in the presence of supercritical carbon dioxide. (o) experimental data, (−) correlation using the Clapeyron equation.

4.   Conclusions

Solubility of coumarin in supercritical carbon dioxide was experimentally determined at temperatures between 308.15 and 321.15 K, and pressures from 10 to 15 MPa. A crossover pressure region was found. This region is predicted by using the Foster's criteria together with the Chrastil's empirical model for representing solubilities, with an average absolute relative deviation of 5.12%. The presence of a melting point depression for coumarin was experimentally confirmed. The variation observed for the solubilities with temperature and pressure are thus explained by melting of the solid that occurs at high pressures.

Acknowledgements

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