

Research note

Measurement and Correlation of Ibuprofen in Supercritical Carbon Dioxide Using Stryjek and Vera EOS

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Abstract

Ibuprofen solubility in supercritical carbon dioxide was measured using a dynamic apparatus at a pressure between 80 and 140 bars at three different temperatures, 308.15, 313.15 and 318.15 K. The mole fraction of Ibuprofen in fluid phase was in the range of 0.015×10^{-3} - 3.261×10^{-3} at the mentioned operational condition. Modified Mendez-Santiago and Teja equation were used to check the consistency of the experimental data. Results were correlated using the Stryjek and Vera equation of state with the van der Waals 1-parameter (vdW1) and 2-parameters (vdW2) mixing and combining rules. Interaction parameters along with the percentage of the average absolute relative deviation (%AARD) were displayed. Also, the Lydersen group contribution methods were used for predicting the physicochemical and critical properties of the Ibuprofen.

Keywords: *Ibuprofen Solubility, Supercritical Carbon Dioxide, Stryjek and Vera EOS, Mendez-Santiago and Teja Equation*

1- Introduction

Solubility data are essential for an accurate design of the operational conditions and to calculate the concentration of supercritical solution, in order to investigate the feasibility of SCF based processes. Supercritical fluids are useful in a variety of applications as food and pharmaceutical industries. Supercritical fluids have been established as powerful solvents for many non volatile and thermal labile compounds [1-2]. A fluid in the supercritical area has gas-like diffusivity,

viscosity and molecular energy, thus promoting high mass transfer, at least an order of magnitude more than those in liquids. In other words, a small change of operational conditions (pressure and temperature) gives rise to a large change in a supercritical fluid density, in spite of a dense liquid character. Therefore, the solvent properties of a fluid change significantly, with little energy consumption in the supercritical area [3-5].

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Based on the supercritical fluids characteristics, the solubility of a solid component in a supercritical solvent is influenced by the solution pressure and temperature sensitively [6-9].

To predict the solubility of a solute in supercritical fluids, EOS models are widely used. Cubic EOSs are the simplest equations capable of predicting and representing fluid phase equilibrium. Mixing rules are necessary when equations of state are applied to calculate the fluid mixtures thermodynamic properties. Although cubic EOS's are the simplest mathematical models, capable of predicting fluid phase equilibrium, semi-empirical models are often utilized because of their relative ease of application compared to EOS's. These models are commonly based on providing a correlation between solubility and density [10-12]. Current investigation has been organized to obtain Ibuprofen solubility data in supercritical CO₂ in low pressure range (80-140 bars). Results have been drawn as three isotherms (in 308.15, 313.15 and 318.15K). Stryjek and Vera equation of state was used to correlate the experimental data within the 1-parameteric and 2-parameteric van der Waals mixing and combining rules. The Lydersen group contribution method was used in order to determine Ibuprofen physicochemical properties.

2- Experimental method

2.1- Materials

Ibuprofen (Sina Daru, 99.99% purity) was used as the original compound and CO₂ (Roham Gaz, 99.95%) was also used as the solvent. Ethanol (99.8%, Sigma Aldrich) was used in analytical grade form.

2.2- Solubility measurements

The solubility of a solid component in supercritical CO₂ was measured by a dynamic technique for the pressure between 80-140 bars and temperatures of 308.15, 313.15 and 318.15 K. Fig. 1 shows the schematic diagram of the solubility measurement apparatus.

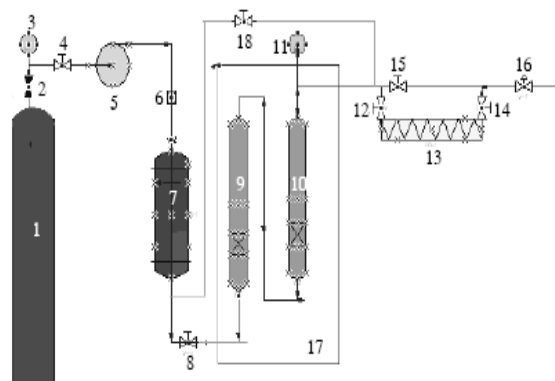


Figure 1. Schematic diagram of the experimental apparatus: 1) gas tank, 2) ball valve, 3,11) pressure gauge indicator, 4,8,12,14,15,18) needle valve, 5) pump, 6) filter 7) pre-heater, 9,10) equilibrium-cell 16) throttling valve , 17) constant temperature bath

Condensed CO₂ was fed to an HPLC pump through a 0.5µm filter, to reach the desired pressure. The compressed fluid entered into a preheating coil contained in a temperature-controlled electronic oven to achieve thermal equilibrium and passed into a solubility cell that was packed with pure Ibuprofen powder. The solute laden purged to the atmosphere in order to ensure the operational condition consistency. The sampling part was a $\frac{1}{8}$ " stainless steel coil installed with two unilateral needle valves. This pass was kept closed during the purging step. After 3 minutes the purge valve was closed and the needle valves were opened orderly. A sample of supercritical solution was trapped into the

sampling pass by closing the needle valves. The sampling equipment (coil and valves) then separated from the system and marinated in the pure ethanol. The valves were then opened and the CO₂ was vented out and all the solute was washed out by ethanol. The ethanol-Ibuprofen solution was prepared for GC test to determine the solute amount. CO₂ amount was calculated by measuring the volume of the sampling equipment and the CO₂ density in the operational pressure and temperature in all runs. Solubility measuring run was performed in triplicate in each operational condition.

3- Results and discussion

3.1- Experimental results

Solubility measuring results for an Ibuprofen-Supercritical CO₂ system are shown in Fig. 2 and are supported by data in Table 1.

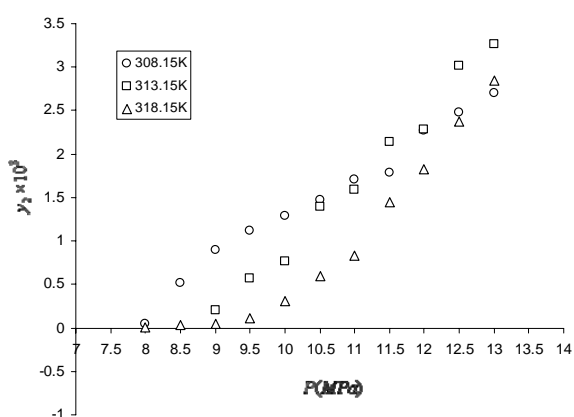


Figure 2. Experimental solubility data obtained in 308.15, 313.15 and 318.15 K and the pressure range of 80-140 bars

According to the experimental results, the mole fraction of ibuprofen in the fluid phase was in the range from 0.015×10^{-3} - $3.261 \times$

10^{-3} . As shown in Fig. 2, solubility is affected by the supercritical solvent pressure and temperature intensively. Pressure increasing at a constant temperature consequently causes the density and the solvent power to increase. In addition, the

Table 1. Experimental molar fraction solubility of Ibuprofen in supercritical CO₂

| T(K) | P(MPa) | y ₂ × 10 ³ | |
|------|--------|----------------------------------|-------|
| 308 | 8 | 0.0428 | |
| | 8.5 | 0.511 | |
| | 9 | 0.903 | |
| | 9.5 | 1.121 | |
| | 10 | 1.287 | |
| | 10.5 | 1.467 | |
| | 11 | 1.713 | |
| | 11.5 | 1.783 | |
| | 12 | 2.269 | |
| | 12.5 | 2.474 | |
| | 13 | 2.705 | |
| | 313 | 9 | 0.198 |
| | | 9.5 | 0.573 |
| 10 | | 0.766 | |
| 10.5 | | 1.393 | |
| 11 | | 1.596 | |
| 11.5 | | 2.142 | |
| 12 | | 2.287 | |
| 318 | 8 | 0.0115 | |
| | 8.5 | 0.028 | |
| | 9 | 0.041 | |
| | 9.5 | 0.109 | |
| | 10 | 0.31 | |
| | 10.5 | 0.602 | |
| | 11 | 0.837 | |
| 11.5 | 1.44 | | |
| 12 | 1.82 | | |
| 12.5 | 2.38 | | |
| 13 | 2.84 | | |

isotherms comparison shows that the solubility power in a constant pressure, changes with the temperature increasingly in lower than 120 bar (~2P_c) and decreasingly in the higher pressure ranges. This result can be interpreted by the iso-fugacity criteria [13]:

$$y_2 = \frac{P_2^{sub}}{P} E \exp\left(\frac{v_2^s(P - P_2^{sub})}{RT}\right) \quad (1)$$

$$E \equiv \frac{\phi_2^{SCF}}{\phi_2^{SCF}}$$

At a constant pressure, both the *E* and *P*₂^{sub} value affect the solubility. At pressures higher than the crossover point (about 120 bar), the effect of *E* is relative to the solid component sublimation pressure intensively. In low pressure ranges, molecular interactions between Ibuprofen and carbon dioxide become severely weak by increasing the temperature. On the other hand, in higher pressure ranges, sublimation pressure is the

more effective factor. Because although the sublimation pressure increases with the temperature, the *E* factor impression by the temperature becomes very weak at high pressures.

3.2- Correlation of solubility using Stryjek and Vera EOS

If the solid phase does not dissolve the SC-CO₂, solute solubility in the CO₂-riched fluid phase at equilibrium can be calculated using the equation (1). The Stryjek and Vera EOS has been selected to calculate ϕ_2^{SCF} , as it has proved to combine the simplicity and accuracy in modeling of several solids solubility in SCFs. The van der Waals mixing rules may be used to calculate the mixture parameter 'a' and 'b' in SV-EOS. Table 2 summarizes the cubic EOS along with the mixing and combining rules and the fugacity coefficient (ϕ_2^{SCF}) used in this work [14].

Table 2. Summary of the cubic EOS, mixing and combining rules and fugacity coefficient

| EOS | | |
|--|--|--|
| $P = \frac{RT}{v-b} - \frac{a}{v(v+b)+b(v-b)}$ | $a = \frac{0.45724R^2T_c^2}{P_c} \times \alpha(T_r, \omega)$ | $b = \frac{0.07780RT_c}{P_c}$ |
| | $\alpha(T_r, \omega) = \left[1 + K(1 - \sqrt{T_r})\right]^2$ | |
| | $K = 0.378893 + 1.4897153\omega - 0.171131848\omega^2 + 0.0196554\omega^3$ | |
| mixing and combining rules | | |
| $a = \sum_i \sum_j y_i y_j a_{ij}$ | | $b = \sum_i \sum_j y_i y_j b_{ij}$ |
| vdW1 | | vdW2 |
| $a_{12} = (1 - k_{12}) \sqrt{a_{11} a_{22}}$ | | $a_{ij} = (1 - k_{ij}) (a_i a_j)^{0.5}$ |
| $b_{12} = \frac{(b_{11} + b_{22})}{2}$ | | $b_{ij} = \frac{(1 - l_{ij})(b_i + b_j)}{2}$ |
| fugacity coefficient | | |
| $\ln \phi_2^{SCF} = -\ln\left(\frac{P((ZRT/P) - b)}{RT}\right) + \frac{Z-1}{b} [b_{22} - (b_{11} + b_{22})l_{12}(1 - y_2)^2] - \frac{1}{2\sqrt{2}RT} \ln \frac{v+b(1+\sqrt{2})}{v+b(1-\sqrt{2})}$ $\times \left[\frac{2a_{22}y_2 + 2\sqrt{a_{11}a_{22}}(1 - k_{12})(1 - y_2)}{b} - \frac{a}{b^2} (b_{22} - l_{12}(b_{11} + b_{22})(1 - y_2)^2) \right]$ | | |

The Correlation is performed by minimizing the objective function of Average Absolute Relative Deviation (AARD) defined by equation (2) [15]:

$$\text{Objective Function} = \text{AARD}(\%) = \frac{100}{N} \sum_{i=1}^N \frac{|y_{i,calc} - y_{i,exp}|}{y_{i,exp}} \quad (2)$$

A trial and error algorithm was provided and encoded for the interaction parameters optimized values computation. The loop was conditioned by 10^{-7} tolerance.

Lydersen group contribution method was also used to predict the physicochemical and critical properties of the Ibuprofen that are presented in Table 3 [16].

Under these conditions, the optimized interaction parameters (k_{12} and l_{12}) showed the best fitting between the experimental data and the calculated values (by SV-EOS and van der Waals mixing rules) (Table 4). A comparison between the correlation results for the SV- EOS at 318.15 K for the two different mixing rules is illustrated in Fig. 3.

Table 3. Physicochemical and critical properties of the ibuprofen and CO₂

| Substance | $T_c(K)$ | $P_c(MPa)$ | ω | $v^s \times 10^6 m^3 mol^{-1}$ | $P^{sub}(Pa) \times 10^{-2}$ | | |
|-----------------|--------------------|-------------------|--------------------|--------------------------------|------------------------------|-------------------|-------------------|
| | | | | | 308.15K | 313.15K | 318.15K |
| Ibuprofen | 749.7 ^a | 2.33 ^a | 0.819 ^a | 182.1 ^b | 4.95 ^c | 8.97 ^c | 16.0 ^c |
| CO ₂ | 304.18 | 7.38 | 0.239 | | | | |

^a Estimated by Lydersen method

^b Estimated by Immirzi and Perini method

^c Estimated by Lyman et al. method

Table 4. Optimized interaction parameter for the modeling of Ibuprofen solubility in CO₂ with the SV-EOS and the van der Waals mixing rules

| Model | Parameter | T(K) | | |
|----------|-----------|--------|--------|--------|
| | | 308.15 | 313.15 | 318.15 |
| SV- vdW1 | k_{12} | 0.093 | 0.084 | 0.090 |
| | AARD% | 16.61 | 10.59 | 22.39 |
| SV- vdW2 | k_{12} | 0.141 | 0.138 | 0.172 |
| | l_{12} | 0.118 | 0.139 | 0.239 |
| | AARD% | 13.93 | 6.41 | 8.95 |

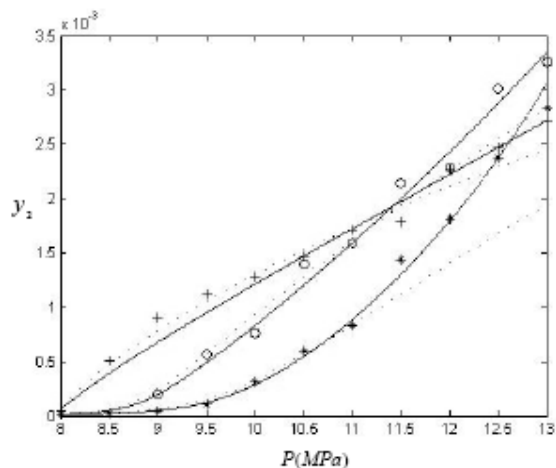


Figure 3. Experimental solubility of Ibuprofen in SC-CO₂ at 308.15(+), 313.15(o) and 318.15K(*) and correlation results obtained with SV EOS using the vdW1 and vdW2

3.3- Modeling with a density-based correlation

In order to check the consistency of experimental data for the solubility of Ibuprofen in SC carbon dioxide as a function of absolute temperature and solvent density, we used the semi-empirical Mendez-Santiago and Teja equation. The modified Mendez-Teja equation can be expressed by the equation (3) [16].

$$T \ln y_2 P = A + B\rho_1 + CT \tag{3}$$

The regression constants and AARD% values are presented in Table 5 in the three isotherms for the model.

The experimental results were plotted in the form of $T \ln y_2 P - CT$ against the supercritical CO₂ density, to test the M-S-T model self-consistency (Fig. 4). The linear behavior shown in Fig. 4 confirms that the measured solid solubility data are consistent at all experimental conditions.

Table 5. Modified Mendez-Santiago-Teja modeling results

| Model | T(K) | A | B | C | AARD% |
|-------|--------|-----------|------|-------|-------|
| M-M- | 308.15 | -14669.88 | 4.03 | 47.79 | 9.10 |
| S-T | 313.15 | | | | 10.66 |
| | 318.15 | | | | 8.76 |

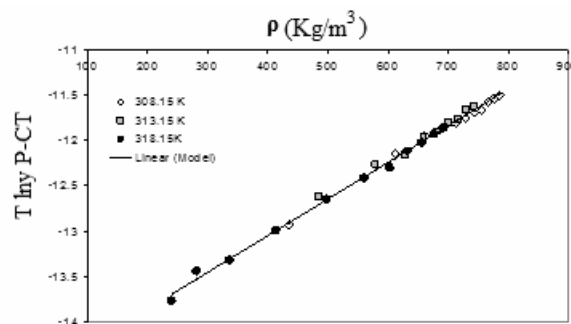


Figure 4. Experimental solubility data for Ibuprofen and values correlated by modified M-S-T model

4- Conclusions

Solubility data conformity by the mathematical models using Stryjek and Vera EOS, was investigated for Ibuprofen in supercritical carbon dioxide. Solubility values were measured in a 308.15, 313.15 and 318.15K and 80-120 pressure range. The experimental data correlate well with the SV EOS model with an average absolute relative deviation (AARD%) of 10–23% along with the vdW1 mixing rule and 6-14% along with the vdW2 mixing rule. The vdW2 mixing rule always produces better correlation results than vdW1, which is probably due to the two available adjustable parameters, which can offer a higher flexibility to the EOS model fitting the experimental solubility data. These data are also well correlated by the semi-empirical model of modified Mendez–Santiago–Teja with an AARD% of 9–11%. The correlated parameters in the semi-empirical models are

feasible for the application of data extrapolation.

5- Nomenclature

| | |
|-----------------------|---|
| A , B and C | adjustable parameters |
| E | enhancement factor |
| ϕ_2^{SCF} | fugacity coefficient of the solute in the fluid phase |
| ρ_1 | supercritical fluid density (kg.m^{-3}) |
| k_{12} and l_{12} | interaction parameters |
| N | number of experimental data |
| P | equilibrium pressure |
| P_2^{sub} | sublimation pressure of solute component |
| T | equilibrium temperature |
| v_2^s | the saturated molar volume of solid solute at the equilibrium temperature |
| y | mole fraction of solid component in supercritical solvent |

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