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Mathematical representation of solute solubility in binary mixture of supercritical fluids by the Jouyban-Acree model

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Applicability of a solution model for calculating the solute solubility in binary mixtures of supercritical fluids at different SCF compositions and pressures was shown using phenanthrene solubility data in supercritical carbon dioxide and supercritical ethane at 313 K and a pressure range of 100–350 bar. The correlation ability of the proposed model was evaluated by fitting all data points and computing error term employing back-calculated solubilities. The prediction capability of the model was assessed by dividing each data set to two subsets, namely training and test subsets. The predicted solubilities using trained models were used to calculate the prediction error term. The results show that both correlative and predictive error terms were less than the experimentally obtained RSD values.

1. Introduction

Supercritical fluids (SCF) are employed in pharmaceutical industry for producing fine drug particles with narrow size distribution, separation of active ingredients and preparing microemulsions and sustained drug delivery systems (Dondeti and Desi 1999). Supercritical carbon dioxide (SC-CO_2) is a very popular fluid for pharmaceutical applications; however, drug's solubility is very low in SC-CO_2. Addition of a supercritical fluid to SC-CO_2 is able to alter the solubility of solutes and was used in industry. The solubility data is required for designing SCF technology and measuring the data by experiments is time-consuming and costly. Mathematical modelling of solubility data in the supercritical fluid mixtures could provide useful information for pharmaceutical engineers to speed up the process of SCF technology design. The aim of this communication is to extend the applicability of a simple and easy to use model for calculating a solute solubility in binary mixtures of SCFs with respect to the pressure and SCF composition. The accuracy of the proposed model is evaluated employing phenanthrene solubility data in SC-CO_2 + ethane taken from Anitescu and Tavlarides (1997).

2. Investigations, results and discussion

The basic solution model, i.e. the combined nearly ideal binary solvent/Redlich-Kister equation (CNIBS/R-K), presented by Acree (1992) was used to correlate different physico-chemical properties in mixed solvent systems; including the solubility of polycyclic aromatic hydrocarbons in non-aqueous binary solvent mixtures (Acree 1995), solubility of drugs in water-cosolvent mixtures (Jouyban-Gh et al. 1999), electrophoretic mobility of ana-

lytes in mixed solvent electrolyte systems (Jouyban-Gh et al. 2000; Jouyban et al. 2003a, 2003b), the instability rate constants in binary solvent systems (Jouyban et al. 2002b), the acid dissociation constants in water-organic solvent mixtures (Jouyban et al. 2002a), the dielectric constant (Jouyban et al. 2004a) and surface tension (Jouyban et al. 2004b) of solvent mixtures. Theoretical basis of the CNIBS/R-K equation for describing the chemical potential of solutes dissolved in mixed solvents (Acree 1992) and acid dissociation constants in aqueous-organic mixtures (Jouyban et al. 2002a) have been provided in earlier papers. As noted above, Jouyban et al. extended the applications of the basic solution model; therefore, it could be called the Jouyban-Acree model (JAM). The model constants of the JAM represent differences in the various solute-solvent and solvent-solvent interactions in the mixture (Acree 1992). Therefore, it should be able to calculate any physico-chemical property (PCP) in mixed solvents, which is a function of solute-solvent and/or solvent-solvent interactions. The general form of JAM is:

$$\ln PCP_m = f_1 \ln PCP_1 + f_2 \ln PCP_2$$
$$+ f_1 f_2 \sum_{i=0}^{2} K_i (f_1 - f_2)^i \qquad (1)$$

Where PCP_m, PCP_1 and PCP_2 are the numerical values of the physico-chemical property of the mixture and solvents 1 and 2, respectively, f_1 and f_2 are the volume (weight or mole) fractions of solvents 1 and 2 in the mixture and K_i represent the model constants calculated using a no intercept least square method (Jouyban-Gh and Hanaee 1997). Equation (1) could be adopted for calculating solute solubility in mixed SCFs at a constant

pressure as:

$$\ln y_m = \phi_1 \ln y_1 + \phi_2 \ln y_2 + \phi_1\phi_2 \sum_{j=0}^{2} M_j(\phi_1 - \phi_2)^j \quad (2)$$

or as Eq. (3) for solubility calculation in binary SCFs at different pressures:

$$\ln y_{m,P} = \phi_1 \ln y_{1,P} + \phi_2 \ln y_{2,P}$$
$$+ \phi_1\phi_2 P \sum_{j=0}^{2} W_j(\phi_1 - \phi_2)^j \quad (3)$$

y in Eqs. (2) and (3) is the mole fraction solubility of the solute, ϕ is the solute free volume/mole fraction of the SCF in the binary mixture, subscripts m, 1 and 2 are SCF 1, 2 and the binary mixture and M and W terms are the model constants. The accuracy of Eq. (3) is evaluated using error term (ET) and calculated by using Eq. (4):

$$ET = \frac{100}{N} \sum \left(\frac{|y_m^{Calculated} - y_m^{Observed}|}{y_m^{Observed}} \right) \quad (4)$$

where N is the number of data points in each set. ET is directly related to experimental relative standard deviation (RSD) values, which is a measure of the reproducibility of the experimental results and enables us to compare the calculation error with RSD.

The experimental solubility data of phenanthrene in SC-CO$_2$ + SC-ethane at different pressures was fitted to Eq. (3) and the following trained model was obtained:

$$\ln y_{m,P} = \phi_1 \ln y_{1,P} + \phi_2 \ln y_{2,P} + 0.00412P\phi_1\phi_2$$
$$- 0.00140P\phi_1\phi_2(\phi_1 - \phi_2)$$
$$- 0.00205P\phi_1\phi_2(\phi_1 - \phi_2)^2 \quad (5)$$

$$R = 0.991, \quad s.e. = 0.02, \quad F = 3104,$$
$$N = 182, \quad ET(\pm S.D.) = 1.23 \pm 1.78\%$$

The higher R (correlation coefficient) and F values and lower standard error of the estimate (s.e.) and ET values reveal that the model is capable of correlating the experimental solubility data with respect to SCF composition and pressure. It should be added that a global fitness test for a multiple regression model was evaluated using the F value, found by splitting the total variations of the response variable into a part due to the regression and a part due to the residual, or error. The numerical value of F is the ratio of the mean squares due to regression to that of the residuals, and the higher the F value is, the more significant the correlation.

To test the prediction capability of the proposed model, the experimental data points in pure SCFs and in mixed SCFs at different compositions and pressures of 350 and 200 bar (total N = 62) were used for training the model that is resulted in the trained Eq. (6) as:

$$\ln y_{m,P} = \phi_1 \ln y_{1,P} + \phi_2 \ln y_{2,P} + 0.00382P\phi_1\phi_2$$
$$- 0.00167P\phi_1\phi_2(\phi_1 - \phi_2)$$
$$- 0.00201P\phi_1\phi_2(\phi_1 - \phi_2)^2 \quad (6)$$

The solubility at other SCFs compositions and pressures was predicted using Eq. (6) and solubility data in pure SCFs where the obtained ET and its standard deviation was $2.24 \pm 1.87\%$ (N = 120). The prediction error could be justified as an acceptable error where the experimen-

tally obtained RSD values for repeated experiments are around 10% (Rehman et al. 2001). In order to further decrease in the number of data points required for the training process, the solubility data at different pressures in pure SCFs was correlated by a reduced form of a recently proposed equation (Jouyban et al. 2002c). This model correlates a solute solubility in a SCF using pressure, temperature (T) and density (ϱ) of SCF as independent variables and is presented as:

$$\ln y = A_0 + A_1 P + A_2 P^2 + A_3 PT + \frac{A_4 T}{P} + A_5 \ln \varrho \quad (7)$$

where $A_0 - A_5$ are the model constants. The accuracy of Eq. (7) was tested using 106 solubility data sets of different compounds in SC-CO$_2$ (Jouyban et al. 2002c). The equation could be reduced to Eq. (8) at a constant temperature:

$$\ln y = J_0 + J_1 P + J_2 P^2 + \frac{J_3}{P} \quad (8)$$

where $J_0 - J_3$ are the model constants. Eq. (8) is able to correlate phenanthrene solubilities in pure SC-CO$_2$ and SC-ethane and the resulted ETs are $0.52 \pm 0.30\%$ and $0.32 \pm 0.23\%$, respectively. Eq. (8) was trained using a minimum number of four solubility data at pressures of 350, 300, 200 and 100 bar in pure SC-CO$_2$ and SC-ethane and the trained models were:

$$\ln y_1 = -2.755 - 6.470 \times 10^{-3}\,P$$
$$+ 7.751 \times 10^{-6}\,P^2 - \frac{314.407}{P} \quad (9)$$

$$\ln y_2 = -4.262 - 4.140 \times 10^{-3}\,P$$
$$+ 4.786 \times 10^{-6}\,P^2 - \frac{324.427}{P} \quad (10)$$

Equations (9) and (10) were replaced with $\ln y_{1,P}$ and $\ln y_{2,P}$ terms in Eq. (6) and the solubility data other than training points was predicted. The obtained ET was $1.81 \pm 1.88\%$ (N = 164).

In conclusion, the low ET values for correlation and prediction studies reveal that JAM is capable of calculating solute solubility in binary SCF at various pressures and could be recommended for industrial applications.

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