Solubility Prediction of Anthracene in Mixed Solvents Using a Minimum Number of Experimental Data

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Received June 7, 2001; accepted October 19, 2001

Numerical methods to predict the solubility of anthracene in mixed solvents have been proposed. A minimum number of 3 solubility data points in sub-binary solvents has been employed to calculate the solvent–solute interaction terms of a well established colsolvency model, *i.e.* the combined nearly ideal binary solvent/Redlich–Kister model. The calculated interaction terms were used to predict the solubility in binary and ternary solvent systems. The predicted solubilities have been compared with experimental solubility data and the absolute percentage mean deviation (APMD) has been computed as a criterion of prediction capability. The overall APMD for 25 anthracene data sets in binary solvents is 0.40%. In order to provide a predictive method, which is based fully on theoretical calculations, the quantitative relationships between sub-binary interaction terms and physicochemical properties of the solvents have been presented. The overall APMD value for 41 binary data sets is 9.19%. The estimated binary interaction terms using a minimum number of data points and the quantitative relationships have then been used to predict anthracene solubility data in 30 ternary solvent systems. The produced APMD values are 3.72 and 15.79%, respectively. To provide an accurate correlation for solubility in ternary solvent systems, an extension to the combined nearly ideal multicomponenet solvent/Redlich–Kister (CNIMS/R-K) model was proposed and the corresponding overall AMPD is 0.38%.

Key words solubility; prediction; cosolvency; anthracene; combined nearly ideal binary solvent/Redlich–Kister model

Mixed solvent systems have a wide range of application in different fields. These include extraction and solubility processes in chemical engineering, solute–solvent interactions in physical chemistry, solubilization of poorly water-soluble drugs in pharmaceutical technology, distribution of environmental contaminants in environmental sciences, dissolving gallstones in clinical sciences[2)]—chemical stability of drugs[3)] and in analytical chemistry.[4)] Our major interest was to study the effects of solvent mixing on the solute solubility and mathematical modelling of experimental solubility data.

Solute solubility data in mixed solvents can provide useful information in process design in the chemical and pharmaceutical industries. Using these data, possible interactions in the solution can be studied. Another application is to provide experimental data for correlation studies, which can be extended to predict unmeasured solubilities. Polycyclic aromatic hydrocarbons, like anthracene, are carcinogenic and mutagenic compounds and their solubilities in mixed solvents are important from an environmental point of view. Since the solubility of anthracene in multicomponent solvent systems have been investigated by our group (see references cited in Tables 1—3), this solute has been chosen as a model compound to represent the applicability of the proposed equations and numerical methods to real experimental data. A similar procedure can be followed in the pharmaceutical industry where solubilization of a poorly water-soluble drug using cosolvents is required.

An accurate mathematical model has been developed to correlate/predict solubility data in mixed solvent systems using a large number of experimental data sets published by our group (see references cited in Tables 1—3).[5)] In addition to this model, a number of other mathematical models for calculating a solute solubility in solvent mixtures have been presented. This includes log–linear,[6)] extended Hildebrand solubility approach,[7)] excess free energy,[8)] mixture response surface method,[9)] phenomenological model,[10)] double log–log,[11)] Margules equations,[12)] and modified Wilson.[13)] The accuracy of most of the models have been compared employing published solubility data in mixed solvent systems.[14,15)] The main disadvantage of these models are that the models employ the curve-fit parameters and in order to compute the curve-fit parameters, one needs to determine the solubility by experiments. This is time consuming and costly, especially when a limited amount of a new drug and/or drug candidate is available. The model discussed in this paper provided more accurate results to correlate solubility data than the literature procedures, however the model needs to use a number of curve-fitting parameters and cannot be employed as a pure predictive model. It is possible to measure solubility in a limited number of different concentrations of the cosolvent in mixed solvent systems and then to carry out prediction at other cosolvent concentrations by an interpolation technique. In this work, the sub-binary interaction terms of the combined nearly ideal binary solvent/Redlich–Kister (CNIBS/R-K) equation have been estimated using a minimum number of experimental data. The estimated model constants have been employed to predict anthracene solubility in binary and ternary solvent mixtures. Also a possible correlation between solute–solvent interaction terms has been investigated in order to provide a predictive model, which is based on theoretical calculations.

Theoretical Section

The CNIBS/R-K is the most accurate model to reproduce the solubility data of non-polar and/or semi-polar solutes in

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non-aqueous (see references cited in a previous paper[14]) and aqueous binary solvents.[15] Its accuracy has been compared with those of other cosolvency models in a recent paper.[15] The model is:

$$\ln X_m = f_1 \ln X_1 + f_2 \ln X_2 + f_1 f_2 \sum_{i=0}^{n} M_i (f_1 - f_2)^i \quad (1)$$

where X_m is the mole fraction solubility in mixed solvent, f_1 and f_2 are the mole/volume fractions of solvents 1 and 2, respectively, X_1 and X_2 denote the mole fraction solubility in pure solvents 1 and 2 and M_i is the model constant estimated by regressing $\ln X_m - f_1 \ln X_1 - f_2 \ln X_2$ against $f_1 f_2 (f_1 - f_2)^i$ terms using a no (zero) intercept least square analysis.[16] The numerical values of n can be varied from 0 to 3 (usually 2). The model can be readily extended to ternary and higher component solvent systems as follows:

$$\ln X_m = f_1 \ln X_1 + f_2 \ln X_2 + f_3 \ln X_3 + f_1 f_2 \sum_{i=0}^{n} B_i (f_1 - f_2)^i + f_1 f_3 \sum_{i=0}^{n} B_i' (f_1 - f_3)^i + f_2 f_3 \sum_{i=0}^{n} B_i'' (f_2 - f_3)^i \quad (2)$$

where f_3 stands for the mole/volume fraction of the solvent 3 in the mixed solvent, B_i, B_i' and B_i'' are the sub-binary interaction terms. It is also possible to include ternary interaction terms (T_i) and obtain:

$$\ln X_m = f_1 \ln X_1 + f_2 \ln X_2 + f_3 \ln X_3 + f_1 f_2 \sum_{i=0}^{n} B_i (f_1 - f_2)^i + f_1 f_3 \sum_{i=0}^{n} B_i' (f_1 - f_3)^i + f_2 f_3 \sum_{i=0}^{n} B_i'' (f_2 - f_3)^i + f_1 f_2 f_3 \sum_{i=0}^{n} T_i (f_1 - f_2 - f_3)^i \quad (3)$$

Equations 1—3 suffer from the limitation that a number of curve-fitting parameters must be calculated employing experimental data points. In order to provide a pure predictive model, the binary interaction terms have been correlated with the solubility parameters of the solvents. This solution avoids employing more training experimental solubility data points. The obtained model is:

$$B_i = K_{1i}(\delta_1 - \delta_s) + K_{2i}(\delta_2 - \delta_s) + K_{3i}(\delta_1 - \delta_s)^2 + K_{4i}(\delta_2 - \delta_s)^2 \quad (4)$$

in which δ_1 and δ_2 are the solubility parameters of solvents 1 and 2, respectively, δ_s is the solute's solubility parameter and K_{1i}—K_{4i} are the model constants.

The average percentage mean deviation (APMD) has been calculated using Eq. 5 as an accuracy criterion.

$$\text{APMD} = \frac{100}{N} \sum \left| \frac{(X_m)_{\text{calculated}} - (X_m)_{\text{observed}}}{(X_m)_{\text{observed}}} \right| \quad (5)$$

where N is the number of data points in each set.

Computational Results and Discussion

The solubilities of anthracene at 3 different compositions and in pure solvents have been fitted to Eq. 1 and the binary interaction terms have been computed. The 3 training data points are selected with equal intervals in the solvent's mole/volume fractions. These points and solubilities in pure solvents 1 and 2 are able to provide accurate predictions using an interpolation technique. The reason for choosing 3 different solvent compositions is due to 3 curve-fitting parameters in Eq. 1. It is obvious that by using more training data points then there will be improvement in the accuracy of predictions. However, this may affect the main aim of this work, *i.e.* prediction based on a minimum number of experiments. Table 1 shows the detail of anthracene solubility in binary solvent mixtures, the solubility parameters, APMD, solubility range, the calculated binary interaction terms and the references to the experimental data. The number of predicted solubility data points in each set for this analysis is ($N-5$). The obtained overall APMD using the solubility in pure solvents and 3 data points from mixed solvent system as a training set is 0.40 %. This low prediction error lies within experimental uncertainty. Therefore, experimental determination of drug solubility in binary solvents at 3 different mixture compositions should be enough to reproduce a solubility curve or optimize the cosolvent concentration, where the researcher should only need to carry out the minimum number of experiments, for example, in the case of scarcity of a new drug and/or drug candidate in the preformulation stage. The estimated binary interaction terms listed in Table 1 have been fitted to Eq. 4 to correlate with solvents' solubility parameters. The solubility parameter of anthracene is equal to 9.5 $(\text{cal/cm}^3)^{1/2}$. The resulted equations are as follows:

$$B_0 = 0.081(\delta_1 - \delta_s) + 0.315(\delta_2 - \delta_s) + 0.159(\delta_1 - \delta_s)^2 - 0.129(\delta_2 - \delta_s)^2 \quad (6)$$

$$B_1 = -0.120(\delta_1 - \delta_s) + 0.047(\delta_2 - \delta_s) - 0.073(\delta_1 - \delta_s)^2 + 0.052(\delta_2 - \delta_s)^2 \quad (7)$$

$$B_2 = 0.048(\delta_1 - \delta_s) - 0.012(\delta_2 - \delta_s) + 0.025(\delta_1 - \delta_s)^2 - 0.031(\delta_2 - \delta_s)^2 \quad (8)$$

The back-calculated binary interaction terms (B_0—B_2) using Eqs. 6—8 have been used to predict the solubility of anthracene in 25 binary systems whose references and also APMD values are shown in Table 1. The number of predicted solubility data points in each set for this analysis is ($N-2$) and the overall the APMD is 6.83%. There is a rank order between prediction capability of the CNIBS/R-K model and the solubility range. The wider the solubility range is the larger the APMD values. To further investigate the applicability of Eqs. 6—8, 16 other anthracene solubility data in published binary solvent systems have been employed. The detail of the data and APMD values are shown in Table 2. The overall APMD is 12.87%. It should be noted that these data sets have not been included to obtain the model constants of Eqs. 6—8.

In order to extend the applicability of the Eqs. 6—8 to ternary solvents, 30 sets of anthracene solubility data in ternary solvent systems have been investigated. The detail of solubility data in ternary solvents, the $\ln X_m$ range and APMD values have been shown in Table 3. Equation 2 showed acceptable APMD using a minimum number of data points (12 points, 3 data points at $f_1 \approx 0.25$, 0.50 and 0.75 for each sub-binary systems and also X_1, X_2 and X_3 values) to estimate the sub-binary interaction terms. The maximum APMD (7.79 %) is observed for anthracene solubility in 2-butoxyethanol+cyclohexane+2,2,4-trimethylpentane and the minimum value (0.80%) is observed for anthracene solubility in 1-propanol+1-butanol+2,2,4-trimethylpentane and the overall APMD is 3.72%. The reported overall APMD for the same ternary solvent systems employing the sub-binary interaction terms calculated using whole binary data points (*ca.* 27 data points for each ternary solvent system) is 1.47%.[17]

Table 1. The Detail of Anthracene Solubility in Binary Solvent Mixtures, Solubility Parameters of Solvents 1 and 2 (δ_1, δ_2), Their References, the Calculated binary Interaction Terms (B_0—B_2) and the APMD Values

No.	Solvent 1	Solvent 2	δ_1	δ_2	APMD[a)]	$\ln X_m$ range	B_0	B_1	B_2	APMD[b)]	N[c)]	Ref.
1	1-Butanol	2-Butoxyethanol	11.29	9.88	0.43	1.55	0.83400	−0.21500	−0.07905	5.20	9	19
2	1-Butanol	1-Propanol	11.29	11.99	0.17	0.30	0.09432	0.00042	0.13100	6.56	9	20
3	1-Butanol	2-Propanol	11.29	11.50	0.19	0.67	0.18700	0.02830	0.23400	5.75	9	20
4	2-Butanol	2-Butoxyethanol	11.13	9.88	0.27	1.87	1.14400	−0.61000	0.34400	10.97	9	19
5	2-Butanol	1-Propanol	11.13	11.99	0.17	0.02	−0.00959	0.01561	−0.02055	7.03	9	20
6	2-Butanol	2-Propanol	11.13	11.50	0.08	0.35	0.09808	0.01462	−0.02838	6.56	9	20
7	Cyclohexane	1-Butanol	8.20	11.29	0.81	0.71	0.70400	−0.17900	0.47300	3.47	9	21
8	Cyclohexane	2-Butanol	8.20	11.13	0.90	1.02	1.27400	−0.23500	−0.31300	9.27	9	22
9	Cyclohexane	2-Butoxyethanol	8.20	9.88	0.33	0.89	1.11700	−0.82900	0.39500	11.58	9	23
10	Cyclohexane	1-Propanol	8.20	11.99	0.43	0.98	1.13600	−0.17000	0.19800	8.89	9	21
11	Cyclohexane	2-Propanol	8.20	11.50	0.51	1.34	1.61200	0.13200	−0.01980	13.83	9	24
12	Heptane	1-Butanol	7.50	11.29	0.28	0.68	0.73700	−0.01515	0.06417	2.26	9	21
13	Heptane	2-Butanol	7.50	11.13	0.22	0.99	1.21700	0.35000	0.09055	4.23	9	22
14	Heptane	2-Butoxyethanol	7.50	9.88	0.72	0.88	0.95200	−0.51500	−0.20300	3.06	9	23
15	Heptane	Cyclohexane	7.50	8.20	1.28	0.06	0.15500	−0.16400	0.20400	5.19	9	25
16	Heptane	1-Propanol	7.50	11.99	0.27	0.98	1.08700	0.05844	0.34600	3.94	7	21
17	Heptane	2-Propanol	7.50	11.50	0.34	1.34	1.52800	0.52500	0.34600	9.39	9	24
18	1-Propanol	2-Butoxyethanol	11.99	9.88	0.23	1.86	1.24600	−0.59100	0.17300	4.82	9	19
19	2-Propanol	2-Butoxyethanol	11.50	9.88	0.31	2.22	1.56600	−0.74800	0.65500	14.28	9	19
20	2,2,4-Trimethylpentane	1-Butanol	6.86	11.29	0.19	0.34	0.55800	−0.14400	0.06029	12.46	9	21
21	2,2,4-Trimethylpentane	2-Butanol	6.86	11.13	0.18	0.65	1.01500	0.20500	0.12700	4.81	9	22
22	2,2,4-Trimethylpentane	2-Butoxyethanol	6.86	9.88	0.86	1.26	0.92800	−0.50800	−0.22400	4.41	9	23
23	2,2,4-Trimethylpentane	Cyclohexane	6.86	8.20	0.13	0.37	0.03111	−0.00518	0.13300	3.93	7	25
24	2,2,4-Trimethylpentane	1-Propanol	6.86	11.99	0.18	0.61	0.83300	0.08881	0.18500	6.29	9	21
25	2,2,4-Trimethylpantane	2-Propanol	6.86	11.50	0.40	0.96	1.24800	0.31700	0.07011	2.50	9	24
				Mean:	0.40					6.83		

a) APMD is calculated using trained model employing $\ln X_1$, $\ln X_2$ and 3 data points of binary mixture. *b*) APMD is calculated using trained model employing $\ln X_1$, $\ln X_2$ and Eqs. 6—8. *c*) N is the number of experimental solubility data points in each set.

Table 2. Detail of Further Anthracene Solubility Data in Binary Solvents, the Solubility Parameter of the Solvents 1 and 2 (δ_1, δ_2) and the Produced APMD for Predicted Solubilities Using Binary Interaction Terms Estimated by Eqs. 6—8

No.	Solvent 1	Solvent 2	δ_1	δ_2	APMD	$\ln X_m$ range	$\ln X_1$	$\ln X_2$	Ref.
1	1-Butanol	Dibutyl ether	11.29	7.79	3.30	1.51	−7.13	−5.62	26
2	1-Butanol	1, 4-Dioxane	11.29	10.01	1.35	2.34	−7.13	−4.79	27
3	1-Butanol	2-Pentanol	11.29	10.59	4.86	0.01	−7.13	−7.13	27
4	2-Butanol	Dibutyl ether	11.13	7.79	4.85	1.82	−7.44	−5.62	26
5	2-Butanol	1, 4-Dioxane	11.13	10.01	24.27	2.66	−7.44	−4.79	27
6	2-Butanol	2-Pentanol	11.13	10.59	27.79	0.31	−7.44	−7.13	28
7	1-Octanol	2-Butoxyethanol	10.23	9.88	17.50	0.56	−6.14	−5.58	19
8	1-Octanol	Dibutyl ether	10.23	7.79	23.47	0.56	−6.14	−5.62	26
9	1-Octanol	1, 4-Dioxane	10.23	10.01	11.06	1.35	−6.14	−4.79	27
10	1-Pentanol	2-Butoxyethanol	10.59	9.88	20.57	1.24	−6.82	−5.58	19
11	1-Propanol	1, 4-Dioxane	11.99	10.01	24.00	2.65	−7.43	−4.79	27
12	1-Propanol	2-Pentanol	11.99	10.59	14.03	0.30	−7.43	−7.13	27
13	1-Propanol	Dibutyl ether	11.99	7.79	19.39	1.81	−7.43	−5.62	26
14	2-Propanol	Dibutyl ether	11.50	7.79	1.54	2.17	−7.80	−5.62	26
15	2-Propanol	1, 4-Dioxane	11.50	10.01	5.90	3.01	−7.80	−4.79	27
16	2-Propanol	2-Pentanol	11.50	10.59	2.07	0.67	−7.80	−7.13	28
			Mean:	12.87					

The number of experimental solubility data points (N) in each set is 9.

In order to provide a pure predictive equation for anthracene solubility in ternary solvents, the sub-binary interaction terms were estimated using Eqs. 6—8 and have been employed to predict anthracene solubility using Eq. 2. The obtained APMD values are shown in Table 3 and the overall APMD is 15.79%. The resulting percentage error is acceptable when it is compared with similar predictive models like universal functional group activity coefficient (UNIFAC) where reported overall APMD was *ca*. 20%.[18)]

In a previous paper,[17)] the accuracy of different cosolvency models to correlate the solubility data in ternary solvents has been compared. The employed models were the extended forms of the CNIBS/R-K model, the Hildebrand solubility approach, the excess free energy model and the mixture response surface method. The obtained overall APMD were 0.84, 0.71, 0.76 and 0.51, respectively.[17)] A novel version of the combined nearly ideal multicomponent solvent/Redlich–Kister, *i.e*. Eq. 3, is proposed to provide more accurate correlation for solubility data in ternary solvents. The resulting overall APMD is 0.38%, which has the lowest APMD among

Table 3. Detail of Anthracene Solubility in Ternary Solvents and the Produced APMD for Different Numerical Analyses

No.	$N^{a)}$	Solvent 1	Solvent 2	Solvent 3	$\ln X_m$ range	APMD$^{b)}$	APMD$^{c)}$	APMD$^{d)}$	APMD$^{e)}$	APMD$^{f)}$	Ref.
1	19	1-Butanol	Heptane	Cyclohexane	0.43	1.86	1.11	11.86	0.20	0.81	29
2	19	1-Butanol	2,2,4-Trimethylpentane	Cyclohexane	0.44	2.10	1.49	8.78	0.20	0.29	30
3	19	2-Butanol	Heptane	Cyclohexane	0.62	2.12	1.74	18.35	0.40	1.02	29
4	19	2-Butanol	2, 2, 4-Trimethylpentane	Cyclohexane	0.58	1.67	2.05	14.75	0.37	0.51	30
5	19	2-Butoxyethanol	Cyclohexane	1-Propanol	1.16	5.49	1.63	25.24	0.71	0.98	31
6	19	2-Butoxyethanol	Cyclohexane	2-Propanol	1.29	6.54	1.59	31.42	0.29	1.11	31
7	19	2-Butoxyethanol	Cyclohexane	Heptane	0.62	6.44	3.22	20.88	0.33	1.37	32
8	19	2-Butoxyethanol	Cyclohexane	2, 2, 4-Trimethylpentane	0.73	7.79	1.21	17.58	0.31	0.90	32
9	19	2-Butoxyethanol	Heptane	1-Propanol	1.17	6.21	1.48	24.51	0.70	1.34	31
10	19	2-Butoxyethanol	Heptane	2-Propanol	1.31	7.43	1.25	30.19	0.53	1.75	31
11	19	2-Butoxyethanol	1-Propanol	1-Butanol	1.12	4.34	1.20	12.62	0. 40	1.00	33
12	19	2-Butoxyethanol	1-Propanol	2-Butanol	1.15	6.24	1.69	15.04	0.23	0.59	33
13	19	2-Butoxyethanol	2-Propanol	1-Butanol	1.32	5.62	1.42	17.97	0.43	0.99	33
14	19	2-Butoxyethanol	2-Propanol	2-Butanol	1.35	7.02	1.75	19.90	0.39	0.82	33
15	19	1-Propanol	1-Butanol	Cyclohexane	0.71	2.56	1.34	8.31	0.39	0.49	34
16	19	1-Propanol	1-Butanol	Heptane	0.65	2.98	1.36	7.90	0.62	1.22	35
17	19	1-Propanol	1-Butanol	2, 2, 4-Trimethylpentane	0.43	0.80	0.84	4.18	0.35	0.57	36
18	19	1-Propanol	2-Butanol	Cyclohexane	0.78	2.42	1.56	10.58	0.32	0.54	34
19	19	1-Propanol	2-Butanol	Heptane	0.71	1.97	0.94	9.80	0.50	0.76	35
20	19	1-Propanol	2-Butanol	2, 2, 4-Trimethylpentane	0.48	1.56	0.47	6.10	0.26	0.39	36
21	19	1-Propanol	Heptane	Cyclohexane	0.64	1.75	1.66	14.61	0.31	0.60	29
22	19	1-Propanol	2, 2, 4-Trimethylpentane	Cyclohexane	0.62	1.52	1.34	13.25	0.39	0.98	30
23	19	2-Propanol	1-Butanol	Cyclohexane	0.90	1.57	1.55	14.34	0.23	0.50	34
24	19	2-Propanol	1-Butanol	Heptane	0.85	4.29	1.72	15.00	0.52	1.36	35
25	19	2-Propanol	1-Butanol	2, 2, 4-Trimethylpentane	0.66	2.00	1.22	10.19	0.19	0.45	36
26	19	2-Propanol	2-Butanol	Cyclohexane	0.96	1.71	1.43	16.65	0.50	0.64	34
27	19	2-Propanol	2-Butanol	Heptane	0.89	5.25	1.89	17.34	0.36	0.67	35
28	19	2-Propanol	2-Butanol	2, 2, 4-Trimethylpentane	0.68	3.35	1.38	12.35	0.19	0.59	36
29	19	2-Propanol	Heptane	Cyclohexane	0.76	3.97	0.99	24.15	0.34	1.22	29
30	19	2-Propanol	2, 2, 4-Trimethylpentane	Cyclohexane	0.82	2.89	1.62	19.80	0.35	0.69	30
					Mean:	3.72	1.47	15.79	0.38	0.84	

a) N is the number of experimental data points. b) APMD is calculated using trained model employing $\ln X_1$, $\ln X_2$, $\ln X_3$ and 9 data points from corresponding sub-binary mixtures. *c*) APMD is calculated using trained model employing $\ln X_1$, $\ln X_2$, $\ln X_3$ and whole data points from corresponding sub-binary mixtures, the values taken from a reference.[9] *d*) APMD is calculated using trained model employing $\ln X_1$, $\ln X_2$, $\ln X_3$ and Eqs. 6—8. *e*) APMD is calculated using the extended form of the combined nearly ideal multicomponent solvent/Redlich–Kister equation, Eq. 3 employing $\ln X_1$, $\ln X_2$, $\ln X_3$ and whole ternary data points. *f*) APMD is calculated using the combined nearly ideal multicomponent solvent/Redlich–Kister equation, Eq. 2 employing $\ln X_1$, $\ln X_2$, $\ln X_3$ and whole ternary data points. These values taken from a reference.[9]

the above-mentioned correlative equations. These correlative expressions provide a means to screen experimental data sets for possible outliers in need of re-determination. Also, it is expected that a more accurate correlative model, provides more accurate predictions using an interpolation technique.

As a general conclusion, the more accurate predictions have been achieved when more experimental data points were employed to estimate the model constants. However, it may affect the main aim of mathematical modelling, for prediction purpose. Here it has been shown that with a minimum number of experiments, one may predict accurate solubilities in mixed solvents. The proposed relationships between the model constants of the CNIBS/R-K equation and the solubility parameters of the solvents and the solute, may provide a pure predictive method for calculating drug solubility in mixed solvent systems. The resulting percentage error is less than similar predictive methods like UNIFAC. Although the solubility of anthracene in mixed solvent systems may not be of direct pharmaceutical interest, a similar procedure may be employed in the pharmaceutical industry where solubilization of a poorly soluble drug is the aim of a project. In addition, non-aqueous solvent mixtures could be used to extract pharmaceutical compounds. After conducting a minimum number of experiments in binary solvents, when a desired solubility is not achieved using binary solvents, the generated data can be employed to predict drug solubility in ternary or higher multicomponent solvent systems. This means a shorter time and also lower cost in the optimisation process for finding the cosolvent concentration in the preformulation stage of a new poorly soluble drug. In extending this computational procedure to predict drug solubility in aqueous ternary solvents, higher APMD values are expected. These higher errors have been shown when the accuracy of the basic model to correlate the solubilities in aqueous and non-aqueous binary solvents has been compared where higher APMD was obtained for aqueous binary mixtures in comparison with non-aqueous binary solvents.[14]

Acknowledgments The authors would like to thank the Australian Department of Education, Training and Youth Affairs and the University of Sydney for providing the IPRS and IPA scholarships.

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