ELSEVIER

International Journal of Pharmaceutics 154 (1997) 245–247

international journal of pharmaceutics

Note

A novel method for improvement of predictability of the CNIBS/R–K equation

A. Jouyban-Gharamaleki [a], J. Hanaee [b,*]

[a] *Department of Pharmaceutical Chemistry, School of Pharmacy, Tabriz University of Medical Sciences, Tabriz, 51664, Iran*
[b] *Department of Pharmaceutical Chemistry, School of Pharmacy, University of Bradford, Bradford, West Yorkshire BD7 1DP, UK*

Received 9 April 1997; accepted 2 May 1997

Abstract

A new method for obtaining the model constants of the combined nearly ideal binary solvent/Redlich–Kister (CNIBS/R–K) equation, via least square analysis has been presented. Predictability of CNIBS/R–K in a previous method and the new one of least square analysis has been compared using some experimental solubility data sets. The results have indicated that the new method improved the predictability of the CNIBS/R–K equation about 63%.

Keywords: Solubility; Cosolvency; Combined nearly ideal binary solvent/Redlich–Kister; Least square analysis

Modelling of experimental solubility data enables researchers to represent mathematical aspects of solubility. According to these models, an unexperienced solute solubility could be predicted in different solvent systems. Several models have been introduced to predict the solute solubility in binary solvent mixtures (Martin et al., 1980; Yalkowsky and Roseman, 1981; Williams and Amidon, 1984; Ochsner et al., 1985; Acree et al., 1991; Acree, 1992; Barzegar-Jalali and Hanaee, 1994; Barzegar-Jalali and Jouyban-Gharamaleki, 1996).

In a recent paper in this journal, the combined nearly ideal binary solvent/Redlich–Kister (CNIBS/R–K) equation, was introduced as the best model for calculating solute solubility in binary solvent mixtures. The author has showed the higher predictability of the model using 8 experimental solubility data sets (Acree, 1996). The similar results were obtained by others (Acree and Zvaigzne, 1991; Barzegar-Jalali and Jouyban-Gharamaleki, 1996; Barzegar-Jalali et al., 1996).

* Corresponding author.

0378-5173/97/$17.00
PII S0378-5173(97)00136-1

Table 1
Comparison of the model constants and $\Sigma(\%D)^2$ obtained from two methods of least square analysis

Solute[a]	The previous method[b]				The new method			
	S_0	S_1	S_2	$\Sigma(\%D)^2$	S_0	S_1	S_2	$\Sigma(\%D)^2$
Methyl *p*-hydroxybenzoate	−0.049	3.424	0.255	318	−0.02377	3.83594	0.10374	214
Ethyl *p*-hydroxybenzoate	−0.591	3.438	0.016	620	−0.63739	3.74114	0.30484	535
Propyl *p*-hydroxybenzoate	−1.402	4.688	1.944	512	−1.24232	4.83991	0.99094	409
Butyl *p*-hydroxybenzoate	−1.244	8.350	5.306	491	−1.31973	8.83333	5.81635	376
Methyl *p*-aminoybenzoate	−0.509	1.709	−0.339	157	−0.43987	1.94333	−0.69467	114
Ethyl *p*-aminoybenzoate	−0.536	2.134	−0.399	261	−0.49290	2.47103	−0.66698	193
Propyl *p*-aminoybenzoate	−1.317	2.427	−0.496	256	−1.31925	2.63848	−0.49802	243
Butyl *p*-aminoybenzoate	−2.073	3.597	2.399	475	−1.87720	3.50774	1.30060	350
				$\Sigma\Sigma(\%D)^2 = 3090$				$\Sigma\Sigma(\%D)^2 = 2437$

[a] Experimental solubility data taken from Rubino and Obeng (1991).
[b] The model constants and S(%D)^2 taken from Acree (1996).

A theoretical basis for CNIBS/R–K was also provided earlier (Acree, 1992). However, improvement of the predictability of the model using a new method for obtaining the model constants could be achieved which is the aim of this communication.

The CNIBS/R–K is one of the theoretical models for calculating the solute solubility in binary solvents and represented by Eq. (1):

$$\ln(X_m) = f_a \ln(X_a) + f_b \ln(X_b) + f_a f_b[S_0 + S_1(f_a - f_b) + S_2(f_a - f_b)^2] \quad (1)$$

where X_m denotes the mole fraction solubility of the solute in the mixed solvents, f_a and f_b are volume fractions of solvents a and b in the absence of the solute, X_a and X_b stand for the mole fraction solubility of the solute in the neat solvents a and b, S_0, S_1 and S_2 represent the model constants which obtained by regressing $\{[\ln(X_m) - f_a \ln(X_a) - f_b \ln(X_b)]/f_a f_b\}$ versus $(f_a - f_b)$ and $(f_a - f_b)^2$ (Acree et al., 1991).

Summed squared percentage deviation, $\Sigma(\%D)^2$, is calculated by Eq. (2) for assessing the accuracy and predictability of the model.

$$\Sigma(\%D)^2 = \Sigma 100[(X_m^{\text{Calculated}} - X_m)/X_m]^2 \quad (2)$$

for overall judgment, sum of $\Sigma(\%D)^2$, i.e. $\Sigma\Sigma(\%D)^2$, is calculated.

Regressing $[\ln(X_m) - f_a \ln(X_a) - f_b \ln(X_b)]$ versus $f_a f_b$, $f_a f_b(f_a - f_b)$ and $f_a f_b(f_a - f_b)^2$ produced more accurate results than the previously reported method. The obtained results for 8 data sets of benzoates in propylene glycol–water mixtures are shown in Table 1.

Comparison of $\Sigma\Sigma(\%D)^2$ for the two methods indicated that the new method improves the predictability of CNIBS/R–K model about 20%. The obtained $\Sigma(\%D)^2$ was less than the previous method and percent of best adherence, PBA, is 100%. It should be noted that PBA is calculated by Eq. (3):

PBA = 100 × (number of data sets producing lower $\Sigma(\%D)^2$ at the new method/total number of studied sets) (3)

Because of some statistical considerations, the yielded constants via two different methods of least square analysis are not same and consequently the predictabilities differ from each other.

For more comparison, 88 experimental data sets whose references cited in our previous paper (Barzegar-Jalali and Jouyban-Gharamaleki, 1996) are fitted to Eq. (1) using two methods of regression. The resulted $\Sigma\Sigma(\%D)^2$ for the previous and the new methods are 60075 and 22074, respectively. So, the improvement of the predictability is about 63% and the PBA value is 91%.

References

Acree, W.E. Jr., 1996. Comments concerning 'Model for solubility estimation in mixed solvent systems'. Int. J. Pharm. 127, 27–30.

Acree, W.E. Jr., 1992. Mathematical representation of thermodynamic properties. Part 2. Derivation of the combined nearly ideal binary solvent (NIBS)/Redlich–Kister mathematical representation from a two-body and three-body interactional mixing model. Thermochimica Acta 198, 71–79.

Acree, W.E. Jr., Zvaigzne, A.I., 1991. Thermodynamic properties of nonelectrolyte solution. Part 4. Estimation and mathematical representation of solute activity coefficients and solubilities in binary solvents using the NIBS and modified Wilson equations. Thermochimica Acta 178, 151–167.

Acree, W.E. Jr., McCargar, J.W., Zvaigzne, A.I., Teng, I.L., 1991. Mathematical representation of thermodynamic properties. Carbazole solubilities in binary alkane + dibutyl ether and alkane + tetrahydropyran solvent mixtures. Phys. Chem. Liq. 23, 27–35.

Barzegar-Jalali, M., Hanaee, J., 1994. Model for solubility estimation in mixed solvent systems. Int. J. Pharm. 109, 291–295.

Barzegar-Jalali, M., Jouyban-Gharamaleki, A., 1996. Models for calculating solubility in binary solvent systems. Int. J. Pharm. 140, 237–246.

Barzegar-Jalali, M., Jouyban-Gharamaleki, A., Hanaee, J., Chookhachizadeh-Moghaddam, M.H., 1996. Comparison of double log–log, mixture response–surface and combined NIBS/Redlich–Kister solubility models. Int. J. Pharm 144, 127–130.

Martin, A., Newburger, J., Adjei, A., 1980. Extended Hildebrand solubility approach: Solubility of theophylline in polar binary solvents. J. Pharm. Sci. 69, 487–491.

Ochsner, A.B., Belloto, R.J. Jr., Sokoloski, T.D., 1985. Prediction of xanthine solubilities using statistical techniques. J. Pharm. Sci. 74, 132–135.

Rubino, J.T., Obeng, E.K., 1991. Influence of solute structure on deviation from log–linear solubility equation in propylene glycol:water mixtures. J. Pharm. Sci. 80, 479–483.

Williams, N.A., Amidon, G.L., 1984. Excess free energy approach to the estimation of solubility in mixed solvent systems: I. Theory. J. Pharm. Sci. 73, 9–13.

Yalkowsky, S.H. and Roseman, T.J., Solubilization of drugs by cosolvents. In: Yalkowsky, S.H. (Ed.), Techniques of Solubilization of Drugs, Dekker, New York, 1981, pp. 91–134.