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Evaluation and Comparison of the Solubility Models for Solute in Monosolvents

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Abstract – The solubility of Cloxacillin sodium in ethanol, 1-propanol, isopropanol, and acetone solutions was measured at different temperatures. The melting property was also tested by using a differential scanning calorimeter (DSC). Then, the solubility data were fitted using Apelblat equation and λh equation, respectively. The Wilson model and NRTL model were not utilized to correlate the test data, since Cloxacillin sodium will decompose directly after melting. For comparison purposes, the four empirical models, i.e., Apelblat equation, λh equation, Wilson model and NRTL Model, were evaluated by using 1155 solubility curves of 103 solutes tested under different monosolvents and temperatures. The comparison results indicate that the Apelblat equation is superior to the others. Furthermore, a new method (named the calculation method) for determining the Apelblat equation using only three data points was proposed to solve the problem that there may not be enough solute in the determination of solubility. The log-logistic distribution function was used to further capture the trend of the correlation and to make better quantitative comparison between predicted data and the experimental ones for the Apelblat equation determined by different methods (fitting method or calculation method). It is found that the proposed calculation method not only greatly reduces the number of test data points, but also has satisfactory prediction accuracy.

Key words: Solubility models, Cloxacillin sodium, Apelblat equation, Probability density function, The statistical frequency

1. Introduction

The solubility of substance is an important physico-chemical property that plays a key role in solute discovery, purification, and designation of the subsequent process. Many solubility data measured by various experimental methods have been reported in recent years [1-6]. However, experimental determination of the solubility is not only tedious but also time-consuming. More importantly, sometimes there are restrictions in the availability of enough solute in the solubility measurements, especially during the early stages of solute discovery investigations in which only a small amount of solute is synthesized or extracted. The solute may be insufficient during this stage since a large number of other tests should also be carried out. Also, solubility data measured by using experimental methods are discontinuous. The data were only tested at certain temperatures. To overcome these shortcomings, the empirical models were developed by many researchers to correlate the solubility of solute.

A number of mathematical models have been proposed by pioneers to provide a faster and easier tool for correlating the solubility of solute. Among these models, Apelblat equation, λh equation, NRTL model, and Wilson model are the most commonly-used solubility models of solute in monosolvents. These models have been widely used for correlating the solubility data of pesticides [7], antidepressants [8], contraceptives [9] polymorphic drugs [10], chemical and pharmaceutical intermediates [3], antiseptics [11], amino acids [12], fine chemical products [13], and some others. Zhu et al. [7] measured the solubility of pymetrozinethe in different monosolvents, and then applied the Apelblat equation and λh equation to correlate the solubility data. It was found that the Apelblat equation is superior to the λh equation in describing the relationship of the solubility data. The solubility of fluoxetine hydrochloride (FH) in 15 pure solvents was tested by Yu et al. [8]. The solubility data were correlated by the Apelblat model, λh model, NRTL model, and Wilson model. Among the four models, the NRTL model presents the best predicted results in the considered pure solvents [8]. The solubility of etonogestrel [9] in ten different monosolvents was tested, and then the measured data were fitted by different models. It is observed that the solubility calculated by the Apelblat model is in good agreement with the experimental data in the ten pure solvents [9]. The solubility data of ganciclovir form I in some pure solvents were measured by Wu and coworkers [10]. These data were fitted by the Apelblat equation, the λh equation, and the NRTL model, respectively. It was found that all these thermodynamic models can correlate the solubility data of ganciclovir form I well. The RAD values are no larger than 3.04×10^{-2}. The solubility of 1,4-dicyanobenzene (DCB) [3] in 17 neat solvents was measured and correlated by the Apelblat equation, λh equation, NRTL model, and Wilson model. It was found that the Apelblat equation presents the best fitting results among these models. The solubility data of propylparaben in polar and apolar solvents were measured by Ouyang and coworkers [11]. The best correlation of solubility versus temperature with the highest accuracy was obtained using the Apelblat model [11]. The

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solubility of L-tryptophan [12] in eight pure solvents was measured and fitted by the Apelblat equation and *λh* equation. It was concluded that the predicted results by Apelblat model are consistent with the experimental data [12]. The solubility of 1-(2-bromo-phenyl)-pyrrole-2,5-dione [13] in 14 pure solvents was determined and mathematically correlated by NRTL model, *λh* equation, Wilson model, and Apelblat equation. The obtained values of the maximum root-mean square deviation and relative average deviation were 51.62×10^{-4} and 4.19×10^{-2}, respectively [13].

In order to illustrate the usage rates of the solubility models mentioned above, taking the solubility data of solute in monosolvent published in the *Journal of Chemical & Engineering Data* that range from volume 64, issue 4, 2019 to volume 65, issue 11, 2020 as an example, it was found that the usage rate of the Apelblat equation, the *λh* equation, the Wilson model and the NRTL model are 100%, 94%, 53% and 64%, respectively. The Apelblat equation and *λh* equation with high usage rate are both the semi-empirical equations. In contrast, NRTL model and Wilson model with lower usage rate can be referred as the activity coefficient models. The equations of these two models are complex and somewhat complicated to be used.

In this paper, the solubility of Cloxacillin sodium in ethanol, 1-propanol, isopropanol, and acetone solutions was measured as a function of temperature. And then the experimental results were respectively analyzed using the Apelblat equation and *λh* equation. The solubility data of solute in monosolvent published in *Journal of Chemical & Engineering Data* that range from volume 64, issue 4, 2019 to volume 65, issue 11, 2020 were selected to verify the four kinds of the most used mathematical models, i.e., Apelblat equation [2], *λh* equation [14], Wilson model [15] and NRTL model [5]. An extensive statistical evaluation of the reliability of the four most used models is presented based on the 1155 solubility curves of 103 solutes in different monosolvents. And then a method used to determine the coefficients of the Apelblat equation is proposed based only on three data points. All these aforementioned experimental data taken from the literature are utilized to validate the reliability of the proposed method.

2. Brief Review of the Solubility Models

2-1. Apelblat equation

A differential relation between the solubility of nonelectrolytes and the temperature was developed by Williamson [16]. Subsequently, the integral form of the Williamson equation was deduced by Apelblat et al. [17-19] (Apelblat equation) assuming that the enthalpy of solution depends linearly on the temperature. The Apelblat equation has been widely applied to model the correlations between the solubility of solute and the temperature due to high accuracy and relative simplicity. The expression of this equation is:

$$\ln x_1 = A + \frac{B}{T} + C \ln T \tag{1}$$

where x_1 expresses the mole fraction solubility of solute in neat solvent, and T is the experimental temperature (unit: Kelvin). The parameters of Apelblat equation are denoted as A, B, and C.

2-2. λh equation

Another approach for modeling the solubility and temperature data was proposed by Buchowski et al. [20,21] (*λh* equation) where only two parameters are necessary. Both the Apelblat equation and *λh* equation can be referred to as semiempirical models. The *λh* equation was developed to investigate the solvent activity along a saturation line and the solubility of hydrogen-bonding solids [15]. This equation can be expressed as:

$$\ln\left[1 + \frac{\lambda(1-x_1)}{x_1}\right] = \lambda h\left(\frac{1}{T} - \frac{1}{T_m}\right) \tag{2}$$

where λ and h refer to the parameters contained in *λh* equation. T_m (unit: Kelvin) denotes the melting point temperature of solute.

2-3. Wilson model

Based on the Flory-Huggins theory, an approach for the activity coefficient was first developed by Wilson [22]. Subsequently, some modifications were presented in Ref. [23]. The Wilson model has been widely utilized in the liquid-solid equilibrium. According to the solid−liquid equilibrium, the relationship between the equilibrium solubility and absolute temperature can be expressed as follows [15]:

$$\ln x_1 = \frac{\Delta_{fus}H}{R}\left(\frac{1}{T_m} - \frac{1}{T}\right) - \ln \gamma_1 \tag{3}$$

where $\Delta_{fus}H$ is the melting enthalpy, R is the universal gas constant, and γ_1 is the activity coefficient of the solute. In the pure solvent system, the activity coefficient γ_1 in Wilson model can be determined by:

$$\ln \gamma_1 = -\ln\left(x_1 + \Lambda_{12}x_2\right) + x_2\left(\frac{\Lambda_{12}}{x_1 + \Lambda_{12}x_2} - \frac{\Lambda_{21}}{x_2 + \Lambda_{21}x_1}\right) \tag{4}$$

where x_2 is the molar fractions of the solvent. Λ_{12} and Λ_{21} are both the model parameters, which can be expressed as:

$$\Lambda_{12} = \frac{V_2}{V_1}\exp\left(-\frac{\lambda_{12} - \lambda_{11}}{RT}\right) = \frac{V_2}{V_1}\exp\left(-\frac{\Delta\lambda_{12}}{RT}\right) \tag{5}$$

$$\Lambda_{21} = \frac{V_1}{V_2}\exp\left(-\frac{\lambda_{21} - \lambda_{22}}{RT}\right) = \frac{V_1}{V_2}\exp\left(-\frac{\Delta\lambda_{21}}{RT}\right) \tag{6}$$

where $\Delta\lambda_{ij}$ stands for the interaction parameter (unit: J/mol), which is related to the interaction energy between components i and j. V_1 and V_2 represent the molar volume of the solute and the solvent, respectively.

2-4. NRTL model

By using the concept of local composition, a method usually named as NRTL model was proposed by Scott [24]. Based on the universal solubility model, which is the solid−liquid phase equilibrium

theory (Eq. (3)), for NRTL model, the activity coefficient of the solute in the pure solvent system can be described as [5]:

$$\ln \gamma_1 = x_1 x_2 \left[\frac{\tau_{21} G_{21}^2}{\left(x_1 + x_2 G_{21}\right)^2} + \frac{\tau_{12} G_{12}^2}{\left(x_2 + x_1 G_{12}\right)^2} \right] \tag{7}$$

$$G_{ji} = \exp\left(-\alpha_{ji} \tau_{ji}\right) \tag{8}$$

$$\alpha_{ij} = \alpha_{ji} \tag{9}$$

$$\tau_{ij} = \frac{g_{ij} - g_{jj}}{RT} = \frac{\Delta g_{ij}}{RT} \tag{10}$$

where Δg_{ij} are the equation parameters concerning the cross-interaction energy. α_{ij} is an adjustable parameter indicating the non-randomness of the solution. Δg_{ij} and α_{ij} in NRTL model may be estimated from limiting activity coefficients or from mutual solubilities.

2-5. Evaluation of the solubility models

The number of undetermined coefficients and physical parameters of the four estimation models are listed in Table 1. It can be seen that the Apelblat equation has three undetermined coefficients, and the other models have two undetermined coefficients. However, except the Apelblat equation, the other three equations contain physical parameters. λh equation contains one physical parameter, i.e., the melting point temperature of solute, T_m. Wilson model contains the melting enthalpy, $\Delta_{fus}H$, the melting point temperature of solute, T_m, and the molar volume of the solute and the solvent, V_1 and V_2. NRTL model contains the melting enthalpy, $\Delta_{fus}H$, the melting point temperature of solute, T_m, and the non-randomness parameter, α. Therefore, the Apelblat equation is more convenient and simpler to use.

3. Experimental Section

3-1. Materials

A white crystalline powder of Cloxacillin sodium (the raw material was provided by Hebei Huari Pharmaceutical Co., Ltd.) was obtained by recrystallization. Its purity, determined by high-performance liquid phase chromatography (Agilent extend-C18 reverse-phase column, HPLC, purchased from Agilent Technologies (China) Co., Ltd.), was found to be higher than 99.0%. The ethanol, 1-propanol, isopropanol, and acetone (purchased from Xi'an Chemical Reagent Factory, China) used for experiments were of analytical reagent grade and dried with anhydrous bitter salt before use.

3-2. Melting properties determination

The melting property of Cloxacillin sodium was determined using the NETZSCH Thermal Analysis DSC204 differential scanning calorimeter and NETZSCH aluminum crucible (purchased from NETZSCH Scientific Instruments Trading (Shanghai) Ltd.). The flow rate of protection gas (nitrogen) was controlled to be 60~80 mL·min^{-1}. The mass of the Cloxacillin sodium added to the crucible was about 5 mg. The measurement temperature ranged from 21 ℃ to 297 ℃, and the heating rate was 10 min· ℃$^{-1}$.

3-3. Solubility measurement

The solubility of Cloxacillin sodium was measured by a synthetic method. The apparatus for the solubility measurements was similar to that described in the literature [25,26]. The solubility apparatus included a jacketed glass vessel maintained at a desired temperature by circulating water from a thermostat. A mercury-in-glass thermometer with an uncertainty of ± 0.05 K was inserted into the inner chamber of the vessel for the measurement of the solution temperature, and the temperature was controlled to within ± 0.1 K of the desired value. Continuous stirring of the solution was achieved with a magnetic stir bar. A condenser was connected with the vessel to prevent the solvents from evaporating. The laser beam monitoring system (consisting of a laser generator, a photoelectric transformer, and a light intensity display) was used to determine the disappearance of the last solute in the solvent at a fixed temperature. At a constant temperature, about 3 mg of Cloxacillin sodium was added to the vessel each time until the strength of the laser beam penetrating the vessel was lower than the initial point and the total amount of the Cloxacillin sodium in the measurement was recorded. An analytical balance with an uncertainty of ± 0.0001 g was used for the measurement of the masses of the solute and solvents. The same experiment was performed three times to obtain the average solubility data.

4. Results and Discussion

4-1. Melting property of cloxacillin sodium

DSC analysis was performed on the crystal of Cloxacillin sodium, and the results are shown in Fig. 1. From Fig. 1, it can be seen that there is an endothermic peak at 181.2 ℃ and an exothermic peak appears at 197 ℃. It can be concluded that the Cloxacillin sodium undergoes decomposition after melting because the endothermic peak is directly followed by the exothermic peak. Therefore, it can be obtained that the melting point of Cloxacillin sodium (T_m) is 181.2 ℃, but its melting enthalpy has no practical significance.

Table 1. Comparison of different models

	fitted Apelblat equation	λh equation	Wilson model	NRTL Model
Number of undetermined coefficients	3	2	2	2
Physical parameters	-	T_m	Δ_{fus}, T_m, V_1 and V_2	Δ_{fus}, T_m and α
Initial application conditions	the enthalpy of solution depends linearly on the temperature	solubility of hydrogen-bonding solids	Based on the concept of local composition	Based on the Flory-Huggins theory

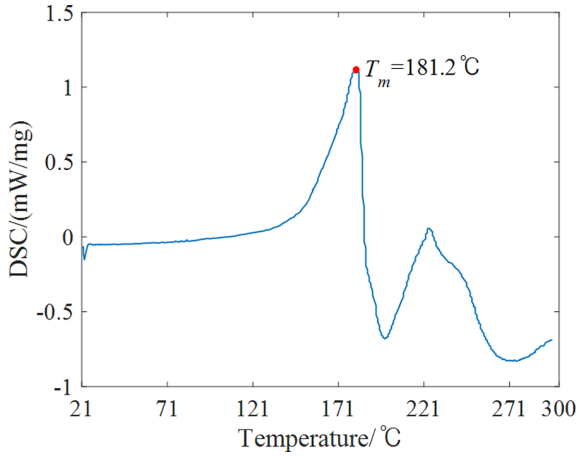


Fig. 1. DSC curve of Cloxacillin sodium.

4-2. Validation of experimental data on the solubility of Cloxacillin sodium

The experimental solubility of Cloxacillin sodium in monosolvents of ethanol, 1-propanol, isopropanol and acetone from 278.15 to 298.15 K is presented in Table 2 and graphically shown in Fig. 2. It 1can be seen from Table 2 and Fig. 2 that the solubility of Cloxacillin sodium in the above four monosolvents increases with the increase of temperature. In addition, the decreasing tendency for mole fraction solubility in these monosolvents is ethanol > 1-propanol > isopropanol > acetone at the same temperature.

In order to predict the solubility values of Cloxacillin sodium at other temperatures, the experimental solubility data were fitted by the Apelblat equation and λh Equation, which are widely used in correlating the solubility of solid-liquid phase. The correlated model

Table 2. Experimental Mole Fraction Solubility Values (10^3 x) of Cloxacillin sodium in monosolvents from 278.15 to 298.15 K (p=0.1 MPa)

T/K	Ethanol	1-propanol	Isopropanol	Acetone
278.15	3.234	0.467	0.00525	0.01493
280.15	3.367	0.685	0.0121	0.02265
283.15	3.692	0.893	0.0265	0.02573
285.15	3.916	0.936	0.0538	0.04426
288.15	4.274	1.246	0.118	0.04154
290.15	4.727	1.263	0.132	0.04905
293.15	5.004	1.587	0.159	0.07458
295.15	5.358	1.694	0.189	0.07608
298.15	6.292	1.994	0.267	0.1002

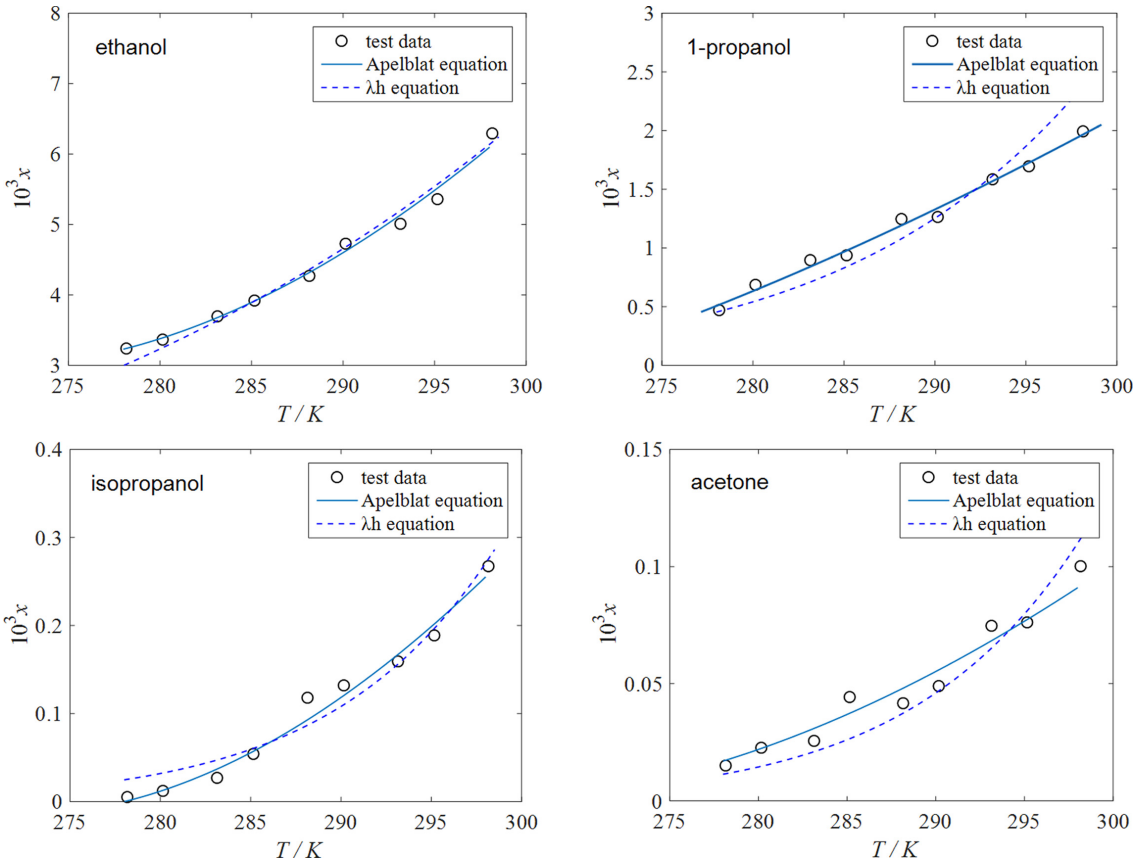


Fig. 2. Mole fraction solubility (x) of Cloxacillin sodium in different monosolvents at elevated temperatures.

Table 3. Fitting Parameters of the Apelblat Model and *λh* equation for Cloxacillin sodium in monosolvents

Solvents	Apelblat model					*λh* equation			
	A	B	C	10^2 RAD	R^2	λ	*h*	10^2 RAD	R^2
ethanol	-561.17	21728.34	84.81	1.51	0.9935	0.1718	16938.2	2.75	0.9756
1-propanol	1934.85	-88563.80	-288.55	4.93	0.9902	6.274	1088.2	10.99	0.8569
isopropanol	10287.82	-458193.12	-1537.39	9.88	0.9773	25.73	385.7	76.56	0.9554
acetone	1364.06	-65672.63	-202.37	10.04	0.9479	5.753	1635.1	17.91	0.8952

parameters and the relative average deviation (RAD) of each the Apelblat equation and *λh* equation are all listed in Table 3. The fitted solubilities of Cloxacillin sodium in monosolvents are also drawn in Fig. 2. Here, the RAD is defined as [3]:

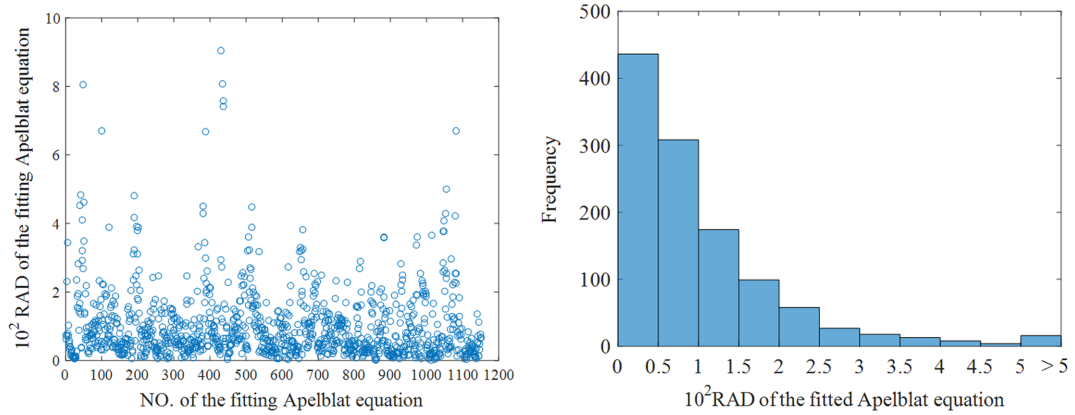
$$RAD = \frac{1}{N}\sum_{i=1}^{N}\left|\frac{x_i - x_i^{cal}}{x_i}\right| \quad (11)$$

where N is the number of tested data for a certain experimental condition. x_i and x_i^{ca} are the tested and calculated mole fraction solubility, respectively. It can be seen from Fig. 2 and Table 3, that the prediction results of the Apelblat equation are better than the *λh* equation. The greater the solubility of Cloxacillin sodium, the better the prediction results of Apelblat equation.

4-3. Model comparison using the test data collected from the literature

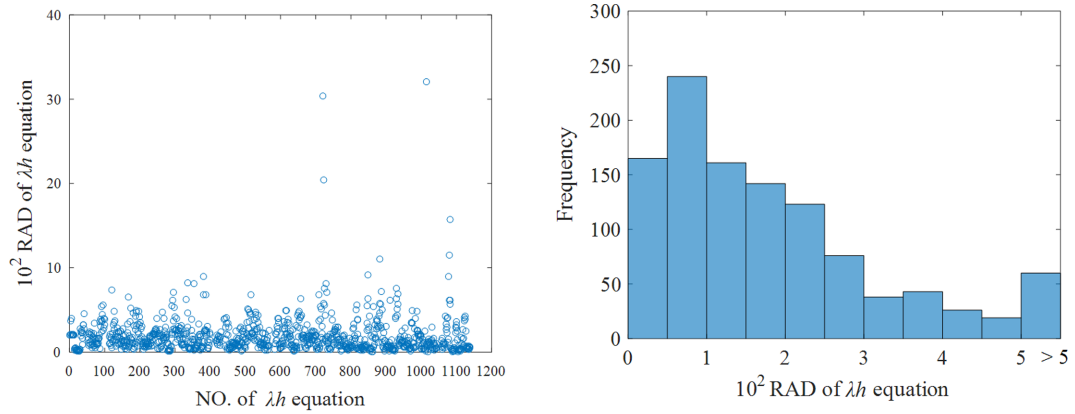
1155 solubility curves of 103 solutes tested in different monosolvents were further studied in the present paper. These solutes cover 44 chemical and pharmaceutical intermediates, 44 drugs (including pesticides, antidepressants, contraceptives and polymorphic drugs), 2 antiseptics, 3 amino acids, and 10 fine chemical products. The temperature range of the solubility data mentioned above is from 272.95 K to 348.85 K. The relevant information of 103 solutes mentioned above and their solubility determination methods are summarized in Appendix A.

It can be seen from the Refs. [2-13,15,25,27-109] that the four empirical models (Apelblat equation, λh equation, NRTL model, and



(a) the value of RAD (b) statistical analysis of RAD

Fig. 3. Values of the RAD for the fitted Apelblat equation.



(a) the value of RAD (b) statistical analysis of RAD

Fig. 4. Values of the RAD for the *λh* equation.

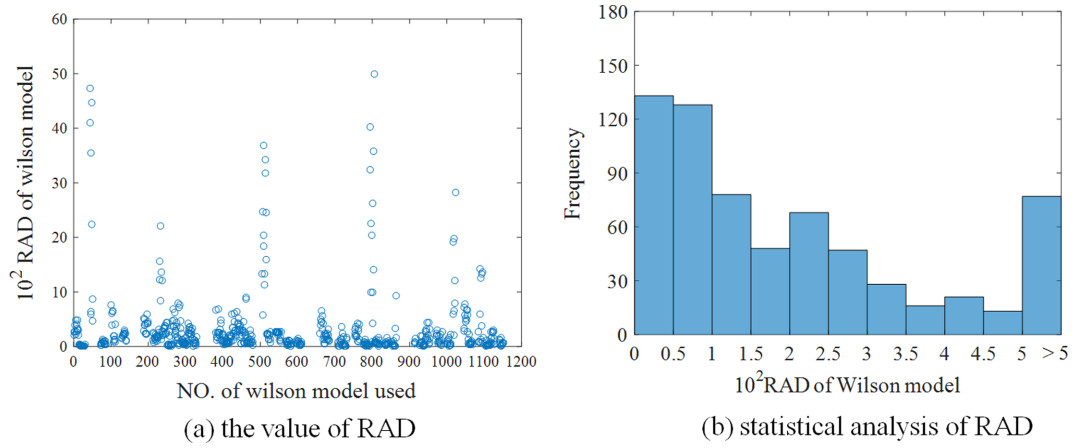


Fig. 5. Values of the RAD for the Wilson model.

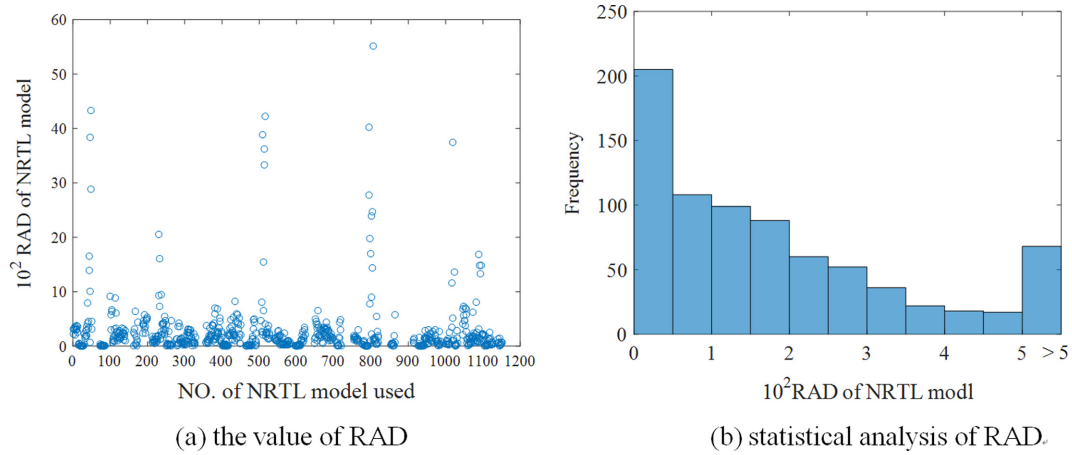


Fig. 6. Values of the RAD for the NRTL model.

Wilson model) shown in the above section are the most frequently used methods to correlate the solubility of solute with the temperature. Here, the solubility data listed in Table A1 were utilized to compare the accuracy and reliability of these empirical models. And the values of RAD were used to evaluate the accuracy and reliability of the prediction results. It can be seen from Eq. (11), the smaller the value of RAD, the higher the prediction accuracy of the model. The values of the RAD for all the considered materials are illustrated in Figs. 3~6(a) for fitted Apelblat equation, λh equation, NRTL model, and Wilson model, respectively. It is important to point out that all the RAD values used to compare the different thermodynamic models were directly taken from the original literature. A statistical analysis of the estimation errors was carried out to quantify the estimation accuracy of the considered models based on the RAD values. The frequency of the estimation for the four discussed models is also illustrated in Figs. 3~6(b). In these figures, the abscissa and ordinate are the values of the RAD and frequency, respectively.

It can be seen from Figs. 3~6(a) that the scattered range of RAD values calculated based on the fitted Apelblat equation is the minimum. The maximum RAD value is less than 10% for the fitted Apelblat equation. In contrast, the maximum RAD values calculated by using λh equation, Wilson model, and NRTL model are about 30%, 50%, 60%, respectively. Besides, it can be seen from the statistical results in Fig. 3~6(b) that the statistical quantity of the four models decreases with the increase of RAD value in the range of 0~5%. When it is greater than 5%, the *λh* equation has a little statistical quantity. The NRTL model and the Wilson model have a similar statistical quantity. As a result, it is clearly shown that the fitted Apelblat equation presents the best estimations.

Based on the RAD, an error criterion, *E*(*s*), is defined as follows to evaluate the capability of the estimation models:

$$\mathrm{E(s)} = \frac{\text{Number of data falling within } 0 \le \mathrm{RAD} \le \mathrm{s}}{\text{Number of total data}} \tag{12}$$

Equation (12) shows that the closer the E(s) is to unity, the better the estimation is. The values of E(0.05) and E(0.1) for different thermodynamic models are both listed in Table 4. It can be seen from Table 4 that the value of E(0.05) for the fitted Apelblat equation is 99.2%, which is the closest to unity among the four considered models. The value of E(0.05) for *λh* equation is 95.0%, which takes the second place. The value of E(0.05) for Wilson model is 88.2%, which is the lowest among these considered models. The value of

Table 4. Comparison of different models

	fitted Apelblat equation	λh equation	Wilson model	NRTL model	calculation Apelblat equation
E(0.05)	99.2%	95.0%	88.2%	91.2%	96.3%
E(0.1)	100%	99.4%	94.3%	96.4%	99.4%

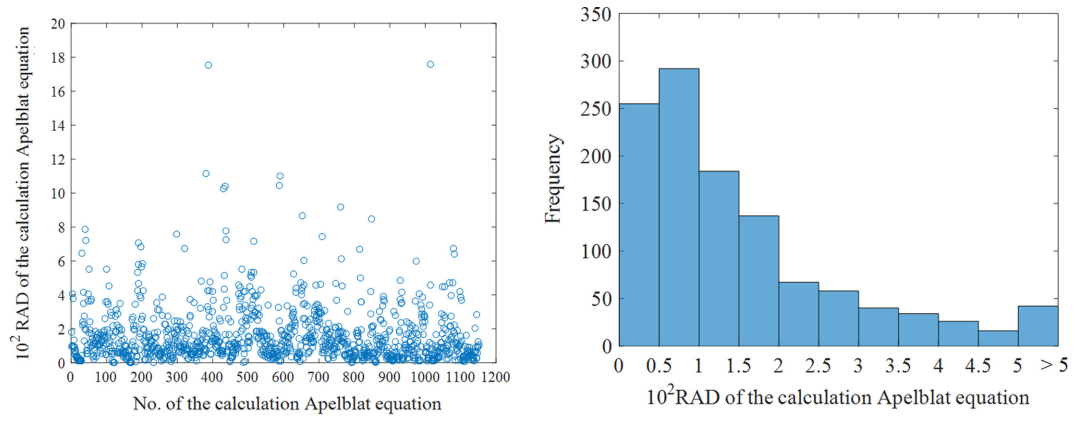
E(0.05) for NRTL model is 91.2%, which is somewhat better than the Wilson Model. Similarly, the same trend can also be observed for the value of E(0.1). The values of E(0.1) are equal to 100%, 99.4%, 96.4%, 94.3% for the fitted Apelblat equation, λh equation, NRTL model, and Wilson model, respectively. It can be concluded that the fitted Apelblat equation presents the best estimations. In other words, the fitted Apelblat equation can correlate the solubility of nonelectrolytes in mono-solvent and the temperature well. In contrast, the predictions for the NRTL model and Wilson model are both somewhat scattered.

4-4. Calculation method for determining the coefficients of the Apelblat equation

As can be seen from the above section, the fitted Apelblat equation presents satisfactory correlations for the 1155 solubility curves of 103 solutes tested in different monosolvents. About ten test data points are necessary to determine the three undetermined coefficients contained in the fitted Apelblat equation. Unfortunately, only a small amount of solute may be synthesized in the early stages of solute discovery investigations, which presents restrictions on the availability of enough solute to be used in the solubility measurements. A simpler solubility curve determination method is desirable, considering the amount of time and effort required to obtain the solubility characteristics in different solvents. Therefore, in the present study, a calculation method is proposed to determine the Apelblat equation by using only three test data points. The three tested solubility data corresponding to the lowest temperature, the middle temperature and the highest temperature are selected to solve the Apelblat equation based on the fact that the Apelblat equation can correlate the test results very well. Here, this method is named as the calculation method, and the Apelblat equation determined using this method is called the calculation Apelblat equation, which corresponds to the fitted Apelblat equation obtained by the fitting method. Based on the proposed calculation method, the calculation Apelblat equation was used to solve the solubility data at other temperatures and compare with the experimental results of 103 Solutes mentioned in above section.

The values of the RAD for all the considered materials and the frequency of the estimation for the calculation Apelblat equation are illustrated in Fig. 7(a) and Fig. 7(b), respectively. Meanwhile, the E(0.05) and E(0.1) for the calculation Apelblat equation are also listed in Table 4. It can be seen from Fig. 7 that maximum RAD values of the calculation Apelblat equation are less than 20%. Most of the data points are less than 5%. It can be seen from Table 1 that the value of E(0.05) for the calculation Apelblat equation is 96.3%, which is higher than for the λh equation, NRTL model and Wilson model. The value of E(0.1) is 99.3%. From the values of RAD and E(s), it can be seen that the calculation Apelblat equation can present reliable prediction results.

The prediction ability of the Apelblat equation was also evaluated by using the error criterion, E(s), based on the scatter band in which the percentage of the RAD falling within a given scatter band was calculated. In order to further capture the trend of the correlation and have a better quantitative comparison between predicted data and the experimental ones, the probability analysis was applied to evaluate the estimation errors. The comparisons for Apelblat equation determined by the fitting method and the calculation method are presented in the format of fitted probability density function (PDF) for the estimation errors. Here, the log-logistic distribution function was chosen as the probability density function, which is given by [110]:



(a) the value of RAD (b) statistical analysis of RAD

Fig. 7. Values of the RAD for the calculation Apelblat equation.

$$f(z)=\frac{\beta\alpha^{\beta}z^{\beta-1}}{\left(\alpha^{\beta}+z^{\beta}\right)^{2}},\ z>0,\ \alpha>0;\beta\geq 1, \tag{13}$$

where α is a scale parameter and β is a shape parameter. The corresponding distribution function can be given by:

$$F(z)=\frac{z^{\beta}}{\alpha^{\beta}+z^{\beta}}\ \ z>0,\ \alpha>0,\beta\geq 1, \tag{14}$$

For the statistical research, each data set was first sorted in ascending order, and then each data point was associated to its mean rank. After that, each data set was fitted using the log-logistic distribution function. The cumulative probability P_f of the predicted data was evaluated by the mean rank method as:

$$F(z)=P_f=\frac{i}{I+1} \tag{15}$$

where i is the rank number, and I is the total number of solubility data. Here, the prediction error is defined as follows:

$$Z=P_e=\frac{x^{cal}}{x_1} \tag{16}$$

Equation (16) shows that the estimation is non-conservative if the P_e value is larger than unity. Otherwise, the conservative estimation will be obtained when the P_e value is less than unity. The closer the value of P_e is to unity, the more accurate the estimation is. The optimum values of the scale parameter, α, and shape parameter, β, were determined by using the least squares method. The curvilinear lines shown in Fig. 8 indicate the fitting results. The optimum results of α and β and the correlation coefficient R^2 are also listed in this figure. R^2 of the two methods are both higher than 0.987. Hence, the fitting results are good for both methods. And then, the best-fitted distributions are illustrated in Fig. 9. It can be seen that the two curves in Fig. 9 are not much different and almost coincide. This means that the proposed calculation method not only greatly reduces the number of test data points, but also has satisfactory prediction accuracy.

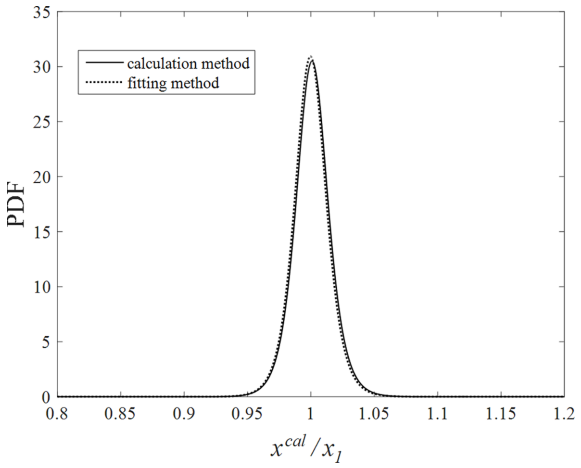
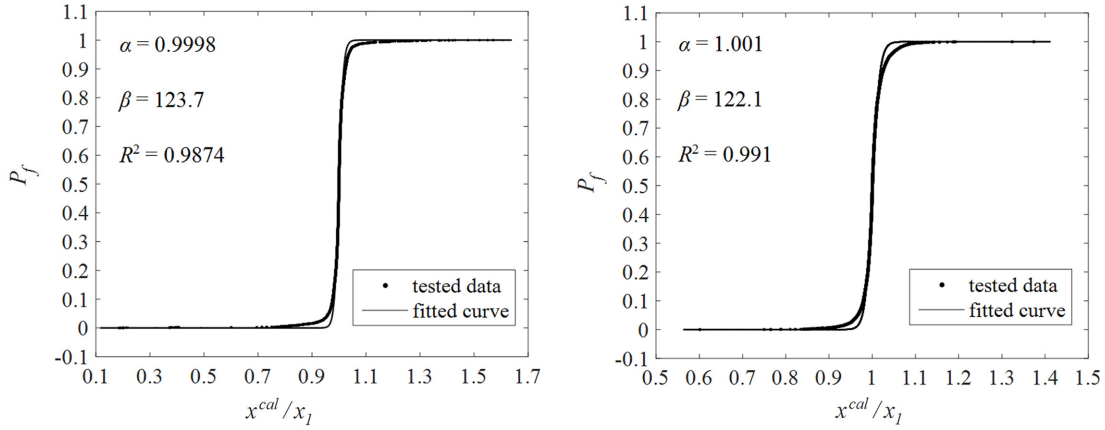


Fig. 9. Probability density functions of the considered estimation methods.

4. Conclusions

The prediction ability of the four frequently used solubility models (Apelblat equation, λh equation, NRTL model, and Wilson model) were compared by using the value of RAD, the statistical frequency, and their undetermined coefficients as well as physical parameters. It was found that the Apelblat equation presents the best predictions, followed by λh equation, NRTL model, and Wilson model. More precisely, the E(0.05) and E(0.1) values of the Apelblat equation are 99.2% and 100%, respectively. And the maximum RAD value of this model is less than 9.05%.

Based on the fact that the Apelblat equation can correlate the solubility data well, a new method is proposed by only using three data points to determine the parameters contained in Apelblat equation. The log-logistic distribution function in the PDF was used to further capture the trend of the correlation and has a better quantitative comparison between predicted data and the tested ones for Apelblat equation determined by different methods (fitting method or calculation method). In contrast to the fitting method, the proposed calculation method can also present satisfactory results. The proposed



(a) the fitting method (b) the calculation method

Fig. 8. Estimates of the considered estimation method (the curvilinear lines show the fit of log-logistic distribution).

calculation method not only greatly reduces the number of test data points, but also has satisfactory prediction accuracy.

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Nomenclature

A, B, and C	: Parameters contained in Apelblat equation
N	: Number of tested data
P_f	: Cumulative probability
P_e	: Prediction error
R	: Universal gas constant
T	: Experimental temperature
T_m	: Melting point temperature of solute.
V_1 and V_2	: Molar volume of the solute and the solvent, respectively
x_1	: Mole fraction solubility of solute in neat solvent
x_2	: Molar fractions of the solvent
α	: Scale parameter
α_{ij}	: Adjustable parameter indicating the non-randomness of the solution
β	: Shape parameter
γ_1	: Activity coefficient of the solute
λ and h	: Parameters contained in λh equation
Δg_{ij}	: Equation parameters concerning the cross-interaction energy
$\Delta\lambda_{ij}$	: Interaction parameter
$\Delta_{fus}H$	: Melting enthalpy
Λ_{12} and Λ_{21}	: Model parameters contained in Wilson model

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Appendix A

The relevant information of 103 solutes used in the present study and their solubility determination methods are listed in Table A1.

Table A1. Information of 103 Solutes and Solubility Determination Methods

Chemicals	CAS registry numbers	Solvents	Solubility determination methods
MOCA[2]	101-14-4	1,4-dioxane, ethanol, n-propanol, EG, isopropanol, water, isobutanol, n-butanol, acetonitrile, DMF, ethyl acetate, methanol, DMA	general shake-flask technique and HPLC
1,4-Dicyanobenzene[3]	623-26-7	methanol, ethanol, n-propanol, isopropanol, acetone, ethyl acetate, ethyl formate, methyl acetate, cyclohexanone, cyclopentanone, tetrahydrofuran, 2-butanone, acetonitrile, chloroform, 2-pentanone, dichloromethane, diethyl ether	gravimetric method
Thiabendazole[4]	148-79-8	methanol, ethanol, n-propanol, n-butanol, isopropanol, isobutanol, acetone, butanone, methyl acetate, ethyl acetate, n-butyl acetate, acetonitrile	gravimetric method
Pidotimod[5]	121808-62-6	water, methanol, ethanol, isopropanol, n-butanol, acetone, acetonitrile, DMF, benzylalcohol	a dynamic method
Sarafloxacin Hydrochloride[6]	91296-87-6	methanol, isopropanol, ethanol, 1-butanol, acetonitrile, n-hexane, ethyl acetate, N,N-dimethylformamide	gravity method
4-(Bromomethyl)-2(1H)-quinolinone[33]	4876-10-2	methanol, ethanol, n-propanol, isopropanol, n-butanol, 2-butanone, acetonitrile, DMF, toluene, NMP, DMSO, 1,4-dioxane	isothermal saturation method
Fluoxetine Hydrochloride[8]	59333-67-4	methanol, ethanol, n-propanol, i-propanol, n-butanol, i-Butanol, s-butanol, n-pentanol, i-pentanol, acetone, 2-butanone, cyclohexanone, acetonitrile, tetrahydrofuran, chloroform	gravimetric method
2-Acrylamide-2-methylpropanesulfonic Acid[34]	15214-89-8	methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, cyclohexane, 1,4-dioxane, EG, ethyl acetate, acetonitrile, n-heptanol, acetone, toluene	isothermal saturation technique
Propylparaben[11]	94-13-3	water, ethanol, methanol, 1-propanol, isopropanol, 1-butanol, acetone, ethyl acetate, methyl acetate, isobutanol, butyl acetate, acetonitrile	shake-flask method
Benzanilide[35]	93-98-1	N,N-dimethylformamide, tetrahydrofuran, butanone, acetone, ethyl acetate, dichloromethane, n-butanol, diethyl ether, n-propanol, acetonitrile, ethanol, methanol, isobutanol, isopropanol, toluene, carbon tetrachloride	the static equilibrium method
2-Nitrophenylacetic Acid[36]	3740-52-1	EG, water, iso-butanol, isopropanol, n-butanol, n-propanol, cyclohexane, methano, acetonitrile, ethyl acetate, 1,4-dioxane, DMF, ethanol	shake-flask method
Ticagrelor[37]	274693-27-5	methanol, ethanol, n-propanol, isopropanol, 1-butanol, isobutanol, n-octanol, cyclohexanone, 2-butanone, toluene, acetonitrile, ethyl acetate	isothermal dissolution equilibrium method
7-Azaindole[38]	271-63-6	ethanol, isopropanol, n-propanol, methanol, EA, acetone, acetonitrile, n-hexane, THF	gravimetric method
Zonisamide[39]	274693-27-5	methanol, ethanol, n-propanol, isopropanol, 1-butanol, ethylacetate, acetonitrile, cyclohexanone, 2-butanone, toluene, 1,4-dioxane, DMF	isothermal dissolution equilibrium method
Nitazoxanide[340]	55981-09-4	Methanol, Ethanol, n-propanol, Isopropanol, 1-butanol, ethyl acetate, Acetonitrile, 2-butanone, Toluene, NMP, DMF, 1,4-dioxane	the isothermal saturation method
γ-Pyrazinamide[341]	98-96-4	methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, acetone, acetonitrile, 1.4-dioxane, methyl acetate, n-propyl acetate, ethyl acetate, water	dynamic method
Benorilate[42]	5003-48-5	methanol, ethanol, n-propanol, isopropanol, 1-butanol, toluene, ethyl acetate, 2-butanone, NMP, DMF, acetonitrile, 1,4-dioxane	isothermal saturation method
3,5-Dibromo-4-hydroxybenzaldehyde[15]	2973-77-5	ethyl acetate, ethanol, water, isobutanol, DMSO, isopropanol, n-pentanol, EG, n-octanol, cyclohexane, methanol, acetonitrile, DMF, n-butanol, 1,4-dioxane, n-propanol	shake-flask method26
Etonogestrel[9]	54048-10-1	Ethanol, Isopropanol, THF, methyl acetate, DMF, n-propanol, ethyl acetate, n-butanol, acetone	gravimetric method
2-Amino-6-chlorobenzoic Acid[27]	2148-56-3	Ethanol, n-propanol, isopropanol, EG, n-heptanol, acetonitrile, Toluene, cyclohexane, isobutanol, ethyl acetate, n-butanol, 1-octanol, NMP, Water	shake-flask technique
Monobenzone[28]	103-16-2	methanol, ethanol, n-propanol, isopropanol, acetone, acetonitrile, n-hexane, n-octanol, ethyl acetate, 1,4-dioxane, n-butanol, DMF, NMP, cyclohexane, water	isothermal method
2-Benzimidazolone[29]	615-16-7	methanol, ethanol, 1-propanol, isopropyl alcohol, 1-butanol, 2-butanol, isobutyl alcohol, methyl acetate, ethyl acetate, propyl acetate, 2-butanone, 1,4-dioxane	gravimetric method
Bisphenol A[30]	80-05-7	DMF, formamide, acetone, 1,4-dioxane, cyclohexanone, ethyl acetate, methyl acetate, acetonitrile, ethanol, methanol, 1-propanol, 1-butanol, 2-propanol, 2-butanol	the laser dynamic method
Chlorpropamide[31]	94-20-2	ethanol, n-propanol, isopropanol, n-butanol, isbutanol, 2-butanol, n-pentanol, isopentanol, ethyl acetate, propyl acetate, isopropyl acetate, butyl acetate, amyl acetate, methyl propionate	the laser dynamic method

Table A1. continued

Chemicals	CAS registry numbers	Solvents	Solubility determination methods
4-Nitrophenylacetic Acid[32]	104-03-0	methanol, ethanol, n-propanol, isopropanol, EG, acetonitrile, cyclohexane, n-butanol, ethyl acetate, isobutanol, water, DMF, DMA	shake-flask method
Gramine[43]	87-52-5	methanol, ethanol, n-propanol, isopropanol, n-butanol, acetone, toluene, acetonitrile, ethyl acetate, 1,4-dioxane, n-octanol	isothermal equilibrium method
3-Bromo-2-Methylbenzoic Acid[44]	76006-33-2	tetrahydrofuran, dimethyl formamide, methanol, ethyl acetate, ethanol, acetonitrile, water, cyclohexane	gravimetric method
Nisoldipine[45]	63675-72-9	ethanol, 1-propanol, acetonitrile, ethyl acetate, 2-propanol, toluene, 1-butanol, cyclohexane, water	isothermal saturation method
2-Chloromethyl-4-methylquinazoline[46]	109113-72-6	n-hexane, acetone, cyclohexane, acetonitrile, tetrahydrofuran, ethyl Acetate, n-propanol, ethanol, isopropanol, butyl alcohol	gravimetric method
N-Acetyl-l-leucine[47]	1188-21-2	methanol, ethanol, n-propanol, 2-butanol, isopropanol, n-butanol, isobutanol, acetone, methyl acetate, ethyl acetate, propyl acetate, acetonitrile	gravimetric method
Isatoic Anhydride[48]	118-48-9	methanol, ethanol, 1-propanol, isopropyl alcohol, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, acetone, 2-butanone, acetonitrile, 1,4-dioxane	gravimetric method
Cetirizine Hydrochloride[49]	83881-52-1	acetonitrile, ethanol, acetic acid, sulfolane	isothermal saturation method
Deferiprone[49]	30652-11-0	acetonitrile, ethanol, ethyl acetate	isothermal saturation method
5,7-Dibromo-8-hydroxyquinoline[50]	521-74-4	methanol, ethanol, n-propanol, isopropanol, n-butanol, ethyl acetate, DMA, DMF, NMP, acetone, toluene, 1,4-dioxane, 2-butanone	shake-flask method
Bezafibrate[51]	41859-67-0	methanol, ethanol, n-propanol, iso-propanol, n-butanol, iso-butanol, sec-butanol, 1-pentanol, iso-pentanol, ethyl acetate, n-propyl acetate, n-butyl acetate, methyl propionate, methyl ethyl ketone, cyclohexanone, acetonitrile	laser dynamic method
3,5-Dinitrosalicylic Acid[52]	609-99-4	ethanol, n-propanol, isopropanol, n-butanol, isobutanol, 1,4-dioxane, acetonitrile, ethyl acetate, EG, cyclohexane, DMF, NMP, DMSO, water	shake-flask method
Lanosterol[53]	79-63-0	methanol, ethanol, n-propanol, isopropanol, acetone, acetonitrile, DMF, DMSO, ethyl acetate	isothermal saturation method
2-Methoxy-4-nitroaniline[54]	97-52-9	methanol, ethanol, n-propanol, isopropanol, n-butanol, EG, ethyl acetate, acetonitrile, NMP, DMSO, water, 1,4-dioxane	shake-flask method
5,5-Dimethylhydantoin[55]	77-71-4	water, methanol, ethanol, 1-propanol, isopropyl alcohol, 1-butanol, isobutyl alcohol, 2-butanol, 1-pentanol, ethyl acetate, propyl acetate, acetonitrile	gravimetric method
N,N-Dibenzylhydroxylamine[56]	621-07-8	methanol, ethanol, n-propanol, n-butanol, acetone, ethyl acetate, dichloromethane, acetonitrile, isopropanol, n-octanol, cyclohexanone, 1,2-dichlorobenzene, toluene, isobutanol, n-pentanol, 1,2,4-trichlorobenzene, tetrahydrofuran	gravimetric analysis method
Mesotrione[57]	104206-82-8	methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, 1-pentanol, methyl acetate, ethyl acetate, butyl acetate, cyclohexane, MTBE	gravimetric method
Bisacodyl[58]	603-50-9	methanol, ethanol, n-propanol, isopropanol, 1-butanol, 1,4-dioxane, DMF, NMP, ethyl acetate, acetone, acetonitrile, toluene	isothermal saturation method
Lamotrigine[59]	84057-84-1	1-propanol, isopropanol, 1-butanol, isobutanol, acetone, ethyl propionate, methyl acetate, ethanol, methyl isobutyl ketone, n-pentanol, water, 2-butanol	static method
4-Chloro-2-nitroaniline[60]	89-63-4	methanol, ethanol, n-propanol, isopropanol, n-butanol, EG, acetonitrile, cyclohexane, 1,4-dioxane, ethyl acetate, water, NMP	shake-flask method
Amprolium Hydrochloride[61]	137-88-2	methanol, ethanol, isopropanol, n-propanol, n-butanol, i-butanol, n-octanol, acetone, ethyl acetate, 1,4-dioxane, acetonitrile, cyclohexanone	isothermal saturation method
3-Bromo-4-Hydroxybenzaldehyde[62]	2973-78-6	methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, n-pentanol, octanol, EG, cyclohexane, ethyl acetate, acetonitrile, DMF, DMSO, 1.4-dioxane, water	shake-flask method
5-Chloro-8-hydroxyquinoline[63]	130-16-5	Ethyl Acetate, Toluene, DMF, NMP, Acetonitrile, 1,4-dioxane	isothermal saturation method
5,7-Dichloro-8-hydroxyquinoline[63]	773-76-2	Ethyl Acetate, Toluene, DMF, NMP, Acetonitrile, 1,4-dioxane	isothermal saturation method
Phenylphosphonic Acid[64]	1571-33-1	Methanol, Ethanol, n-Propanol, Isopropyl Alcohol, 1-Butanol, 1-Pentanol, 1-Hexanol, 1-Heptanol, 1-Octanol, Acetone, 1,4-Dioxane, 2-Methoxyethanol, 2-Ethoxyethanol, 2-Propoxyethanol, 2-Butoxyethanol	isothermal saturation method
Sulfanilamide[65]	63-74-1	acetone, methanol, ethanol, 1-propanol, 2-propanol, 2-butanol, 1-butanol, benzene, Water, 1-octanol, ethyl acetate, toluene	gravimetric method
o-Toluenesulfonamide[66]	88-19-7	methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, n-pentanol, isopentanol, acetone, ethyl acetate, acetonitrile, cyclohexanone, cyclopentanone, methyl acetate, ethyl formate, dichloromethane	gravimetric analysis method
Marbofloxacin[67]	115550-35-1	Methanol, Ethanol, Acetonitrile, Isopropanol, n-Propanol, n-Butanol, Ethyl Acetate, tert-Amyl Alcohol, Acetone, Toluene, Tetrahydrofuran, 1,4-Dioxane	dynamic laser monitoring method

Table A1. continued

Chemicals	CAS registry numbers	Solvents	Solubility determination methods
2-Chloronicotinic Acid[68]	2942-59-8	Methanol, Ethanol, n-Propanol, Isopropanol, DMF, 1,4-Dioxane, NMP, Ethyl acetate, Acetone, Water, Acetonitrile, Cyclohexane	isothermal saturation method
Sancycline[69]	808-26-4	methanol, ethanol, n-propanol, isopropanol, 1-butanol, isobutyl alcohol, n-octanol, cyclohexane, n-hexane, 1,4-dioxane, acetonitrile, ethyl acetate	isothermal saturation method
β-Arbutin[70]	497-76-7	methanol, ethanol, propanol, isopropanol, butyl alcohol, isobutanol, ethyleneglycol, acetone, 2-butanone, acetonitrile, methyl acetate, ethyl acetate	gravimetric method
2,6-Dichloro-4-nitroaniline[71]	99-30-9	methanol, ethanol, n-propanol, isopropanol, n-butanol, EG, acetonitrile, cyclohexane, 1,4-dioxane, ethyl acetate, NMP, water	shake-flask method
Phenformin[72]	114-86-3	methanol, ethanol, n-propanol, isopropanol, EG, ethyl acetate, Acetonitrile, NMP, n-butanol, DMF, Isobutanol, Water, DMSO, 1,4-dioxane	shake-flask method
N,N'-Diethylthiourea[73]	105-55-5	methanol, ethanol, n-propanol, isopropanol, n-butanol, sec-butyl alcohol, n-pentanol, acetone, butanone, methyl acetate, ethyl acetate, acetonitrile	gravimetric method
Gastrodin[74]	62499-27-8	ethanol, n-propanol, isopropanol, acetone, acetonitrile, ethyl acetate, cyclohexanone, 1,4-dioxane, toluene, 1-butanol, cyclohexane	isothermal saturation method
2-Oxindole[75]	59-48-3	acetonitrile, DCM, 1,4-dioxane, ethyl acetate, acetone, toluene, methanol, ethanol, 2-propanol, THF, 1-butanol, 1-propanol	synthetic method
1,3,5-Trifluoro-2,4,6-triiodobenzene[25]	84322-56-5	methanol, ethanol, acetone, toluene, EtOAc, acetonitrile, THF, 1-propanol, 2-propanol, n-hexane, 1,4-dioxane, 1,2-dichloroethane	synthetic method
Amidinothiourea[76]	2114-02-5	Methanol, Ethanol, 1-Propanol, 2-Propanol, 1-Butanol, Acetone, Acetonitrile, Ethyl acetate, Toluene, Cyclohexane, 1,4-Dioxane, Ethanol	isothermal saturation method
L-Serine[77]	56-45-1	methanol, ethanol, isopropanol, n-butanol, acetonitrile, ethyl acetate, acetone, water	gravimetric method
1-(2-Bromo-phenyl)-pyrrole-2,5-dione[13]	36817-47-7	methanol, ethanol, n-propanol, isopropanol, EG, acetone, acetonitrile, NMP, n-butanol, DMF, isobutanol, water, cyclohexane, DMSO	shake-flask method
3-Hydroxy-2-nitropyridine[78]	15128-82-2	n-hexane, methanol, ethanol, n-propanol, isopropanol, ethyl acetate, acetonitrile, acetone, tetrahydrofuran, water	gravimetric method
Dimethyl Terephthalate[79]	120-61-6	methanol, ethanol, n-propanol, i-propanol, n-butanol, i-butanol, ethyl acetate, i-propyl acetate, n-propyl acetate, n-butyl acetate, n-amyl acetate, methyl propionate, Acetone, Methyl ethyl ketone, cyclohexanone, acetonitrile, chloroform	laser dynamic method
Dienogest[80]	65928-58-7	methyl tert-butyl ether, xylene, 1-propanol, tetrahydrofuran, ethanol, ethyl acetate, isopropanol, acetone, acetonitrile, dimethylformamide, methanol, water	isothermal saturation method
2-Aminobenzamide[81]	88-68-6	methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, n-pentanol, acetone, ethyl acetate, acetonitrile, tetrahydrofuran, isopentanol, n-hexanol, n-octanol, methyl acetate	gravimetric analysis method
5-Aminotetrazole[82]	4418-61-5	methanol, ethanol, n-propanol, isopropanol, 1-butanol, acetonitrile, acetone, ethyl acetate, toluene, 1,4-dioxane, NMP, DMF	isothermal saturation method
5-Methyl-2-pyrazinecarboxylic Acid[83]	5521-55-1	methanol, ethanol, n-propanol, isopropanol, 1-butanol, acetone, 2-butanone, toluene, acetonitrile, ethyl acetate, 1,4-dioxane, water	isothermal saturation method
L-Tryptophan[12]	73-22-3	methanol, ethanol, 1-butanol, acetone, acetonitrile, ethyl acetate, isopropanol	gravimetric method
3-Nitrophthalonitrile[84]	51762-67-5	Methanol, Ethanol, n-Propanol, Isopropanol, EG, Acetone, Toluene, NMP, n-Butanol, Ethyl Acetate, Isobutanol, Water	isothermal saturation method
3-Methyl-6-nitroindazole[85]	6494-19-5	tetrahydrofuran, ethyl acetate, acetone, DMF, acetonitrile, N-propanol, ethanol, water	static equilibrium method
(2E)-1-(3-Pyridyl)-3-(dimethylamino)-2-propen-1-one[86]	123367-26-0	methanol, n-propanol, dimethylformamide, acetone, 1,4-dioxane, ethyl acetate, tetrahydrofuran, cyclohexane	gravimetric method
Buprofezin[87]	69327-76-0	methanol, ethanol, isopropanol, n-butanol, acetonitrile, n-hexane, ethyl acetate, N,N-dimethylformamide	gravimetric method
2-Mercaptobenzimidazole[88]	583-39-1	Methanol, Ethanol, Acetonitrile, n-Propanol, Isopropanol, 1-Butanol, Acetone, Ethyl Acetate, 1,4-Dioxane, Cyclohexane, Toluene, 2-Butanone	isothermal saturation method
5-Nitrosalicylaldehyde[89]	7-51-8	Methanol, Ethanol, n-Propanol, Isopropanol, 1-Butanol, Acetonitrile, Acetone, Cyclohexanone, Ethyl Acetate, 1,4-Dioxane, Toluene, Water	isothermal saturation method
Musk Ketone[90]	84-14-1	methanol, ethanol, n-butanol, ethyl acetate	isothermal saturation method
Diclazuril[91]	101831-37-2	Methanol, Ethanol, 1-Propanol, 2-Propanol, Acetone, Acetonitrile, Ethyl Acetate, Toluene, DMF, 1-Butanol	isothermal saturation method
Benzenesulfonamide[92]	98-10-2	methanol, ethanol, n-propanol, isopropanol, n-butano, isobutanol, n-pentanol, isopentanol, acetone, ethyl acetate, acetonitrile, cyclohexanone, cyclopentanone, methyl acetate, ethyl formate, dichloromethane	gravimetric analysis method

Table A1. continued

Chemicals	CAS registry numbers	Solvents	Solubility determination methods
3,5-Dinitro-2-methylbenzoic Acid[93]	28169-46-2	1-propanol, 1-butanol, 1-pentanol, 1-hexanol, 1-heptanol, 2-propanol, ethyl acetate, 2-butanol, cyclohexane, toluene, ethanol, acetonitrile, water	shake-flask method
Hydrochlorothiazide[94]	58-93-5	methanol, n-propanol, water, ethyl acetate, ethanol, acetonitrile, isopropanol, 2-butyl alcohol, 1-pentanol, isobutyl alcohol	laser monitoring method
Pymetrozine[7]	123312-89-0	2-Propanol, 1-Butanol, DMSO, DMF, 1,4-Dioxane, NMP	static equilibrium method
o-Nitrophenylacetonitrile[95]	610-66-2	Methanol, Ethanol, n-Propanol, Isopropanol, Acetone, 2-Butanone, Acetonitrile, Toluene, 1,4-Dioxane, Cyclohexane, Isobutanol, Ethyl Acetate, n-Butanol, Acetic Acid, Ethylbenzene, Water	shake-flask method
d-Aspartic Acid[96]	1783-96-6	methanol, ethanol, n-propanol, n-butanol, isopropanol, water, DMF, DMSO, NMP, 1,4-dioxane, EG, acetone	shake-flask method
2-Chloro-5-nitroaniline[97]	6283-25-6	Methanol, Ethanol, n-Propanol, Isopropanol, 1-Butanol, Toluene, NMP, Acetone, 2-Butanone, 1,4-Dioxane, Ethyl Acetate, Acetonitrile	isothermal saturation method
Warfarin Sodium 2-Propanol Solvate [98]	67430-45-9	acetone, ethanol, IPA, water	polythermal method
Mifepristone[97]	84371-65-3	methanol, ethanol, n-propanol, isopropanol, n-butanol, propanone, ethyl acetate, tetrahydrofuran	shake-flask method
Ganciclovir Form I[10]	82410-32-0	Methanol, Ethanol, n-Propanol, Isopropanol, 1-Butanol, Acetonitrile, Acetone, Ethyl acetate, Toluene	isothermal saturation method
Iohexol[100]	66108-95-0	Ethanol, n-Propanol, Isopropanol, n-Butanol, Acetone, Ethyl Acetate, Acetonitrile, 1,4-Dioxane, Cyclohexane, 2-Butanone, DMSO, Toluene	static equilibrium method
4-Aminobenzamide[101]	2835-68-9	water, ethanol, methanol, 1-propanol, isopropanol, 1-butanol, acetone, ethyl acetate, methyl acetate, isobutanol, butyl acetate, acetonitrile	gravimetric method
Quizalofop-p-ethyl[102]	100646-51-3	Methanol, Ethanol, 1-Propanol, 2-Propanol, 1-Butanol, 1,4-Dioxane, DMF, Ethyl Acetate, Toluene, 1-Hexane, Acetonitrile, Acetone	static equilibrium method
Azacyclotridecan-2-one[103]	947−04-6	methanol, ethanol, n-propanol, isopropanol, n-butanol, isobutanol, n-pentanol, ethyl acetate, acetone, toluene, acetonitrile, dichloromethane, 1,2-dichlorobenzene, cyclohexanone, tetrahydrofuran	gravimetric method
2-Cyanoacetamide[104]	107-91-5	DMF, acetone, acetonitrile, methanol, MAC, THF, ethanol, EAC, n-propanol, n-butanol, TCM, DCM, 1,4-dioxane, water	laser dynamic method
2,6-Dimethylnaphthalene[105]	581-42-0	isopropyl alcohol, n-heptane, cyclohexane, ethyl acetate, n-propyl acetate, 2,2,4-trimethylpentane	static equilibrium method
2-Amino-3-methylbenzoic Acid[106]	4389-45-1	Methanol, Ethanol, 1-Propanol, 2-Propanol, 1-Butanol, 2-Butanone, Acetone, 1,4-Dioxane, Acetonitrile, Ethyl Acetate, Toluene, Cyclohexane	isothermal saturation method
1,5-Naphthalenediamine[107]	2243-62-1	Methanol, n-Propanol, Isopropanol, Toluene, Ethyl Acetate, Acetonitrile	isothermal saturation method
1,8-Naphthalenediamine[107]	479-27-6	Methanol, n-Propanol, Isopropanol, Toluene, Ethyl Acetate, Acetonitrile	isothermal saturation method
Indole-3-acetic Acid[108]	87-51-4	methanol, ethanol, n-propanol, isopropanol, n-butanol, ethyl acetate, 1,4-dioxane, DMSO, DMF, acetone, acetonitrile, chloroform	isothermal saturation method
Borneol[109]	507-70-0	acetone, ethanol, p-cymene, p-xylene	gravimetric method
Camphor[109]	76-22-2	acetone, ethanol, p-cymene, p-xylene	gravimetric method
Isoborneol[109]	124-76-5	acetone, ethanol, p-cymene, p-xylene	gravimetric method
Cloxacillin sodium	642-78-4	ethanol, 1-propanol, isopropanol, and acetone	laser dynamic method