Solubilities of Ibuprofen in Different Pure Solvents

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Using a laser monitoring technique, the solubility of ibuprofen in ethanol, 1-propanol, 1-butanol, 1-pentanol, 2-propanol, 2-methyl-1-propanol, 3-methyl-1-butanol, acetone, and ethyl acetate was determined in the temperature range from (283.15 to 318.15) K. The solubility data were correlated with a semiempirical equation. The calculated results of this are proven to show a fine representation of experimental data.

Introduction

Ibuprofen ($C_{13}H_{18}O_2$, molecular weight 206.28, CAS Registry No. 15687-27-1, Figure 1) is a white crystalline powder. Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) derived from propionic acid and is widely used as analgesic and antipyretic, although it is also used for relief of symptoms of rheumatoid arthritis and osteoarthritis in addition to treatment of dysmenorrheal, among other indications.[1] Although ibuprofen is used widely nowadays in therapeutics, the physicochemical information such as solubility for this drug is not abundant; the only knowledge of the solubility is in several solvents.[2−4] For many pharmaceutical purposes, especially in performulation studies, it is necessary to measure the solubility of ibuprofen.[4] In the present work, the solubility of ibuprofen was measured in the temperature range from (283.15 to 318.15) K for various organic solvents using a laser monitoring observation technique. This measurement is much faster and more readily available than the analytical method.[5]

Experimental Section

Materials. A white crystalline powder of ibuprofen with a mass fraction of higher than 0.994 was purchased from JiangXi GuoXing Fine Chemical Industry Co., Ltd., and was prepared by recrystallizing from the solution of ethanol two times. All solvents used for experiments were of analytical reagent grade, and their mass fraction purity was higher than 0.997 from Beijing Chemical Reagent Co.

Apparatus and Procedure. The solubilities were measured at atmospheric pressure by using an apparatus similar to that described in literature.[6−9] The dissolution of the solute was carried out in a jacketed glass vessel which was maintained at the desired temperature. Continuous stirring was achieved with a magnetic stir bar. A calibrated (uncertainty of ± 0.05 K) mercury-in-glass thermometer was inserted into the inner chamber of the vessel. The dissolution of the solute was examined by the laser beam penetrating the vessel. To prevent evaporation of the solvent, a condenser vessel was introduced. The masses of the samples and solvents were weighted using an analytical balance (sartorius CP224S, Germany) with an uncertainty of ± 0.0001 g. During the experiments, the predetermined solvents were placed in the vessel and stirred continuously at a required temperature. Ibuprofen was added to the vessel simultaneously. The laser beam intensity passing through the vessel reached a maximum when the solute dissolved completely. Then, additional solute of known mass {about (0.5 to 5) mg} was introduced into the vessel. This procedure was repeated until the penetrated laser intensity could not return maximum or, in other words, the last addition of solute could not dissolve completely. The interval of addition was 120 min. The total amount of the solute consumed was recorded. The same solubility experiment was conducted three times, and the mean values were used to calculate the mole fraction solubility (x_A) based on the following equation:

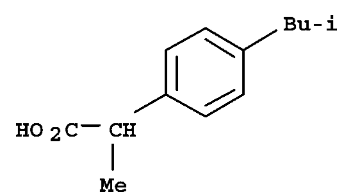

Figure 1. Chemical structure of ibuprofen.

$$x_A = \frac{m_A/M_A}{m_A/M_A + m_S/M_S} \tag{1}$$

where m_A and m_S represent the mass of the solute and solvent, respectively, and M_A and M_S are the molecular weight of the solute and solvent, respectively. The uncertainty of the experimental solubility values is about 2.0 %. The uncertainty in the solubility values can be due to uncertainties in the temperature measurements, weighing procedure, instabilities of the water bath, and excess addition of ibuprofen.

Results and Discussion

The solubility of ibuprofen is listed in Table 1. The relationship between temperature and solubility of the ibuprofen is correlated with the modified Apelblat equation, which is a semiempirical equation:[10,11]

$$\ln x_A = A + \frac{B}{T/\mathrm{K}} + C \ln(T/\mathrm{K}) \tag{2}$$

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Table 1. Solubility (x_A) of Ibuprofen in Different Solvents between (283.15 and 318.15) K

T/K	x_A	$100(x_A - x^{cal})/x_A$	T/K	x_A	$100(x_A - x^{cal})/x_A$
		Ethanol			
285.05	0.1232	−1.22	303.39	0.2319	−0.69
288.65	0.1445	1.87	307.87	0.2698	0.22
293.33	0.1669	−0.06	312.93	0.3158	0.32
298.47	0.1979	−0.40	317.95	0.3657	−0.05
		1-Propanol			
284.17	0.1279	−0.47	303.41	0.2484	−0.52
288.63	0.1522	0.85	307.89	0.2887	0.07
293.35	0.1774	−0.34	313.01	0.3386	−0.12
298.25	0.2112	0.38	318.27	0.3992	0.20
		1-Butanol			
283.97	0.1394	1.36	303.43	0.2652	0.98
288.25	0.1562	−1.92	308.67	0.3114	0.35
293.77	0.1912	−0.21	313.47	0.3607	0.03
298.73	0.2251	−0.22	318.23	0.4155	−0.48
		1-Pentanol			
283.13	0.1336	0.45	303.13	0.2636	−0.08
288.05	0.1579	−0.32	307.91	0.3103	0.81
293.37	0.1902	−0.16	312.57	0.3578	0.34
298.03	0.2219	−0.45	318.15	0.4215	−0.52
		2-Propanol			
282.97	0.1273	0.86	303.57	0.2645	−0.26
288.07	0.1528	−0.92	307.57	0.3051	1.51
293.43	0.1876	−0.27	312.75	0.3505	0.06
298.21	0.2219	−0.18	318.17	0.4051	−0.57
		2-Methyl-1-propanol			
282.89	0.1075	−0.09	303.23	0.2410	−1.12
288.09	0.1343	−0.22	308.17	0.2918	0.38
293.07	0.1660	0.48	313.55	0.3483	−0.26
298.07	0.2022	0.64	317.85	0.4027	0.25
		3-Methyl-1-butanol			
283.57	0.1206	−0.08	303.13	0.2527	−0.28
288.61	0.1480	−0.20	308.17	0.2990	−0.23
293.71	0.1821	0.78	313.31	0.3525	−0.03
297.95	0.2113	0.00	318.83	0.4169	0.22
		Acetone			
283.57	0.1437	0.63	303.25	0.2732	0.48
288.49	0.1684	−1.01	308.07	0.3114	−0.16
293.37	0.1996	−0.35	312.65	0.3516	−0.37
297.87	0.2330	0.77	317.99	0.4051	0.15
		Ethyl Acetate			
283.17	0.1267	0.08	302.75	0.2713	0.44
288.47	0.1584	0.06	307.83	0.3195	−0.03
293.57	0.1935	−0.16	313.07	0.3762	0.08
297.69	0.2254	−0.27	318.45	0.4388	−0.07

Table 2. Parameters of Equation 2 for Ibuprofen and rmsd in Different Solvents

solvent	A	B	C	10^3 rmsd
ethanol	0.289367	−2605.96	1.19778	1.42
1-propanol	−15.7482	−1913.22	3.61609	0.89
1-butanol	−53.5143	−158.355	9.22097	1.89
1-pentanol	−31.1358	−1205.96	5.91192	1.43
2-propanol	105.804	−7348.47	−14.5084	2.09
2-methyl-1-propanol	67.9035	−5987.66	−8.67426	1.35
3-methyl-1- butanol	87.427	−6682.55	−11.6823	0.74
acetone	91.5297	−6480.52	−12.5052	1.28
ethyl acetate	136.171	−8863.89	−18.9399	0.55

where T is the absolute temperature, and A, B, and C are dimensionless constants. The difference between experimental and calculated results is also presented in Table 1. The values of parameters A, B, and C together with the root-mean-square deviations (rmsd's) are listed in Table 2. The rmsd is defined as follows:

$$\mathrm{rmsd} = \left[\sum_{i=1}^{N} \frac{(x_A - x_A^{cal})^2}{N-1}\right]^{1/2} \qquad (3)$$

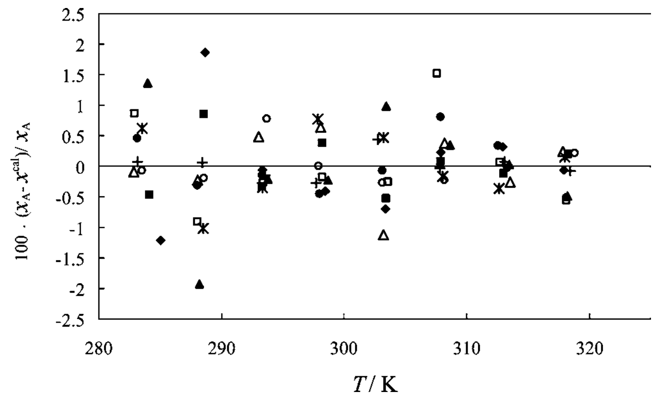

Figure 2. Differences between the experimental solubility and calculated results of ibuprofen in different solvents: ◆, ethanol; ■, 1-propanol; ▲, 1-butanol; ●, 1-pentanol; □, 2-propanol; △, 2-methyl-1-propanol; ○, 3-methyl-1-butanol; ∗, acetone; +, ethyl acetate.

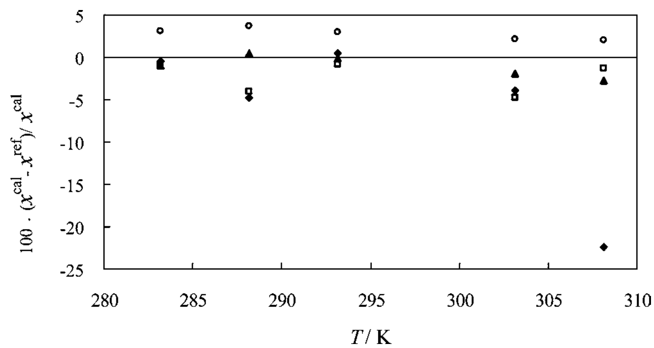

Figure 3. Differences between the calculated solubility of ibuprofen (x^{cal}) and literature data in ref 2 (x^{ref}): ◆, ethanol; ▲, acetone; □, 2-propanol; ○, ethyl acetate.

where x_A^{cal} is the solubility calculated from eq 2, x_A is the experimental value of solubility, and N is the number of experimental points.

From Tables 1 and 2 and Figures 2 and 3, we could draw the following conclusions: (1) The solubilities of ibuprofen in these solvents increase with temperature, but the increment with temperature varies for different solvents. (2) As can be seen in Figure 3, the solubilities of ibuprofen in 2-propanol, acetone, and ethyl acetate show a satisfactory agreement with the literature values, which were determined from (283.15 to 308.15) K. For the solubility in ethanol, the experimental values are consistent with the literature values in the temperature range from (283.15 to 298.15) K, while the solubility in ref 2, $x = 0.2978$ at 308.15 K, is quite larger than the experimental value, 0.2698 at 307.87 K. The solubilities in ethanol are measured three times, and the results agree with each other. (3) The calculated solubilities of ibuprofen in aqueous solutions show good agreement with the experimental values. The experimental solubility and correlation equation in this work can be used in manufacturing and purifying processes of ibuprofen in industry.

Literature Cited

(1) Manrique, J.; Martinez, F. Solubility of Ibuprofen in Some Ethanol+Water Cosolvent Mixtures at Several Temperatures. *Lat. Am. J. Pharm.* **2007**, *26*, 344–354.

(2) Gracin, S.; Rasmuson, A. C. Solubility of Phenylacetic Acid, *p*-Hydroxyphenylacetic Acid, *p*-Aminophenylacetic Acid, *p*-Hydroxybenzoic Acid, and Ibuprofen in Pure Solvents. *J. Chem. Eng. Data* **2002**, *47*, 1379–1383.

(3) Pacheco, D.; Manrique, Y.; Martinez, F. Thermodynamic study of the solubility of ibuprofen and naproxen in some ethanol + propylene glycol mixtures. *Fluid Phase Equilib.* **2007**, *262*, 23–31.
(4) Garzon, L. C.; Martinez, F. Temperature Dependence of Solubility for Ibuprofen in Some Organic and Aqueous Solvents. *J. Solution Chem.* **2004**, *33* (11), 1379–1395.
(5) Hefler, G. T.; Tomkins, R. P. T. *The Experimental Determination of Solubilities*; John Wiley: Chichester, U.K., 2003.
(6) Wang, S.; Wang, J. K.; Yin, Q. X. Measurement and correlation of solubility of 7-aminocephalosporanic acid in aqueous acetone mixtures. *Ind. Eng. Chem. Res.* **2005**, *44*, 3783–3787.
(7) Hao, H. X.; Wang, J. K.; Wang, Y. L. Solubility of dexamethasone dodium phosphate in different solvents. *J. Chem. Eng. Data* **2004**, *49*, 1697–1698.
(8) Li, Q. S.; Liu, Y. M.; Wang, S.; Wu, H.-L. Solubility of D-(−)-*p*-Hydroxyphenylglycine Dane Salt in Mixtures of Methanol and Ethanol. *J. Chem. Eng. Data* **2006**, *51*, 2182–2184.
(9) Ren, G. B.; Wang, J. K.; Yin, Q. X.; Zhang, M. J. Solubilities of proxetine hydrochloride hemihydrate between 286 and 363 K. *J. Chem. Eng. Data* **2004**, *49*, 1671–1674.
(10) Wang, S.; Wang, J. K.; Yin, Q. X.; Wang, Y. L. Light extinction method for solubility measurement. *Chin. Opt. Lett.* **2005**, *3*, 149–151.
(11) Liu, B. S.; Gong, J. B.; Wang, J. K.; Jia, C. Y. Solubility of potassium clavulanate in ethanol, 1-propanol, 1-butanol, 2-propanol, and 2-methyl-1-propanol between 273 and 305 K. *J. Chem. Eng. Data* **2005**, *50*, 1684–1686.

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