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SHORT ARTICLE

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Solubilities of Ursolic Acid and Oleanolic Acid in Four Solvents from (283.2 to 329.7) K

Jie-Ping Fan,*,[†] Tao Kong,[†] Lu Zhang,[†] Sheng Tong,[†] Zhe-You Tian,[†] Yong-Hua Duan,[†] and Xue-Hong Zhang[‡]

[†]School of Environmental and Chemical Engineering and [‡]School of Foreign Language, Nanchang University, Nanchang 330031, China

ABSTRACT: The solubilities of ursolic acid and oleanolic acid in four solvents (methanol, ethanol, 2-propanol, and ethyl acetate) are measured over the temperature range of (283.2 to 329.7) K. The experimental solubility data are correlated by the modified Apelblat equation. The root-mean-square deviation (rmsd) between the experimental value and the calculated value is not more than $1.1267 \cdot 10^{-4}$, so the calculated solubility shows good agreement with the experimental data.

■ INTRODUCTION

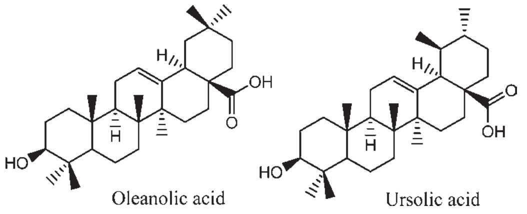
Ursolic acid (UA) and oleanolic acid (OA) (Scheme 1) are ubiquitous pentacyclic triterpene acids in the plant kingdom and medicinal herbs and are an integral part of the human diet.[1] UA is also the main component of protective wax-like coatings of many fruits.[2] They have attracted a lot of attention because of their various biological activities including anti-inflammatory, antiprotozoal, and antimutagenicity properties and cytotoxicity to cancer cells.[3]

UA and OA, which often coexist in many medicinal plants and herbs, have been isolated from more than 120 plant species.[4] They are usually extracted from these plants using various solvents and should be isolated from these extracts for some purpose.[5,6] To obtain a high yield and separation efficiency by selecting the optimal solvent, knowledge of the solubility of UA and OA in various solvents is a prerequisite. Schneider et al. developed a quick method of predicting the solubility of the blend of UA and OA in various solvents using a novel and simple ultraviolet spectroscopy method.[7] In a previous report by Jin et al.,[8] only at 288.15 K, the solubilities of UA and OA were measured in aqueous surfactant solutions, liquid poly(ethylene glycols) (PEG), and solvents of various polarities. Though the solubility of OA in ethanol, 1-butanol, acetone, and water have been measured over the temperature range of (288.3 to 328.3) K,[9] its solubility in 2-propanol, ethyl acetate, and methanol was not listed. Moreover, no reports concerning the solubility of UA in pure organic solvents have been published over temperature range of (283.2 to 329.7) K. So, in this work the solubilities of UA and OA in methanol, ethanol, 2-propanol, and ethyl acetate have been measured by a synthetic method and correlated by the modified Apelblat equation from (283.2 to 329.7) K.

■ EXPERIMENTAL SECTION

Materials. The UA (≥ 98 % purity) and OA (≥ 98 % purity) were purchased from the Shananxi Sciphar Biotechnology Co. Ltd., Shanxi, China. Methanol together with 2-propanol, absolute ethanol, and ethyl acetate (purchased from the Damao Chemical Reagents Co., Tianjin, China) were of analytical reagent grade and were used without further treatment.

Scheme 1. Structure of Oleanolic Acid and Ursolic Acid



Solubility Measurement. The solubility was measured according to a literature method with a little modification.[9,10] A vial with a rubber stopper was used to prepare saturated solutions (about 15 mL) of solute, in which excess solid solute was dissolved in organic solvents. The vial was stoppered, sealed up with tape, and fastened with a rubber band to prevent evaporation of the solvents. Then the vial was placed in a low temperature thermostatic reaction bath (type DFY5/40, China) with an uncertainty of ± 0.1 K. The solution was stirred by an electric magnetic stirrer, and the temperature of the system was determined by a microthermometer (Shanghai, China) with an uncertainty of ± 0.1 K. The vial was allowed to settle for about 48 h to ensure equilibrium and stand for 4 h before sampling. For each vial, three samples of approximately (0.1 to 0.5) mL were withdrawn from the clear saturated solution with preheated glass syringes. The glass syringes with saturated solution were weighed on an analytical balance (type FA1104N, Shanghai, China) with an uncertainty of ± 0.1 mg. To prevent evaporation of solvent during the weighing process, the needle was closed with silicon rubber. The saturated solution was injected into the volumetric flasks (10 mL) immediately to prevent precipitation. After that, the mass of the glass syringes with the remaining solution was

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Table 1. Experimental Mole Fraction Solubility (x_1) of UA in the Four Solvents over the Range (293.6 to 329.7) K

T/K	$10^3 x_1$	$10^3(x_1^c - x_1)$	100δ	$10^3 x_1$	$10^3(x_1^c - x_1)$	100δ
		Methanol			Ethanol	
293.6	0.7229	0.0334	4.6232	0.5137	0.0797	15.5109
300.1	0.8512	−0.0018	0.2068	0.7659	−0.0984	12.8417
305.2	0.9311	0.0022	0.2382	0.7351	−0.0007	0.0908
310.0	1.0244	−0.0024	0.2301	0.7608	0.0444	5.8364
320.1	1.3340	−0.0885	6.6381	1.0457	−0.0627	5.9940
323.2	1.3238	0.0011	0.0834	1.0479	−0.0013	11.9533
329.7	1.4610	0.0511	3.4987	1.1643	0.0319	2.7432
		2-Propanol			Ethyl Acetate	
293.6	1.4439	0.1218	8.4363	0.7771	−0.0665	8.5563
300.1	1.8085	−0.0401	0.0222	0.7712	0.0920	11.9313
305.2	1.9749	−0.0293	0.0149	1.0065	−0.0070	0.6924
310.0	2.1337	−0.0053	0.0025	1.1292	0.0128	1.1346
320.1	2.7303	−0.1600	0.0586	1.5527	−0.0615	3.9623
323.2	2.7470	−0.0238	0.0087	1.6235	−0.0108	0.6659
329.7	2.9544	0.1186	0.0401	1.8646	0.0265	1.4233

Table 2. Experimental Mole Fraction Solubility (x_2) of OA in the Four Solvents over the Range (283.2 to 326.2) K

T/K	$10^3 x_2$	$10^3(x_2^c - x_2)$	100δ	$10^3 x_2$	$10^3(x_2^c - x_2)$	100δ
		Methanol			Ethanol	
283.2	0.3088	0.0479	15.5110	0.7488	0.0728	9.7159
296.2	0.5250	−0.0736	14.0320	0.9757	−0.0258	2.6450
305.2	0.5303	0.0095	1.7939	1.0617	0.0096	0.9004
316.2	0.6690	0.0150	2.2484	1.4550	−0.1904	13.0916
323.2	0.7971	0.0040	0.4974	1.4148	0.0030	0.2131
326.2	0.8460	−0.0054	0.6236	1.3700	0.1222	8.9193
		2-Propanol			Ethyl Acetate	
283.2	0.8033	0.0930	11.5786	1.4792	−0.0097	0.6571
296.2	1.0440	−0.0563	5.3906	1.9600	−0.0485	2.4759
305.2	1.0733	0.0091	0.8499	2.2352	0.0913	4.0831
316.2	1.4430	−0.2039	14.1245	3.0570	−0.0605	1.9804
323.2	1.3607	−0.0066	0.4880	3.5218	0.0214	0.6082
326.2	1.2900	0.1396	10.8200	3.8300	−0.0179	0.4685

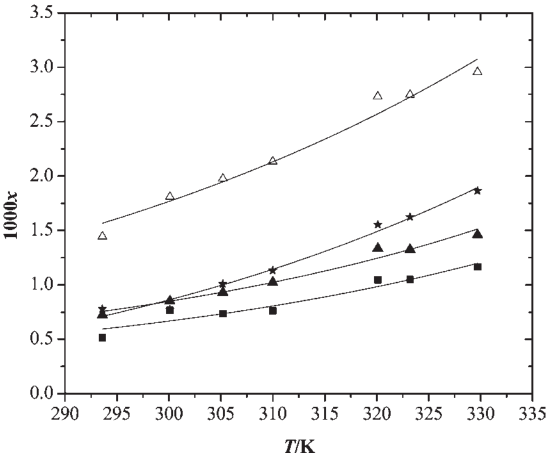

Figure 1. Mole fraction solubility (x) of UA in various solvents at different temperatures (T): △, 2-propanol; ★, ethyl acetate; ▲, methanol; ■, ethanol.

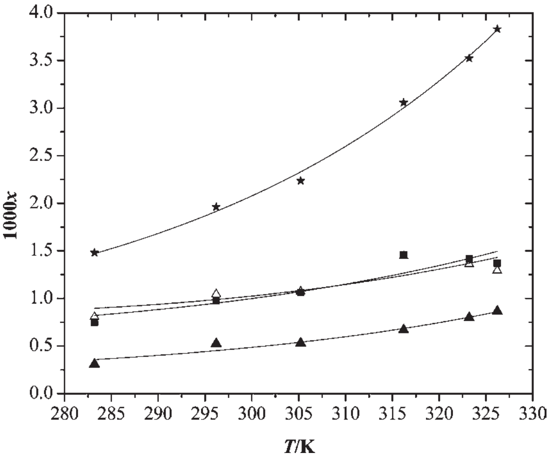

Figure 2. Mole fraction solubility (x) of OA in various solvents at different temperatures (T): △, 2-propanol; ★, ethyl acetate; ▲, methanol; ■, ethanol.

weighed, and the mass of the saturated solution in the volumetric flasks can be determined. The sample solution was diluted to the mark prior to high-performance liquid chromatography (HPLC) determination. Each experiment was repeated at least twice to check the repeatability of the solubility determination, and three samples were taken for each solvent at each temperature. In this work, the measuring relative uncertainty of the experimental solubility value was ± 3 %.

Chromatographic Conditions. The solubilities of UA and OA were determined by using HPLC (Agilent 1100, Agilent Technologies, USA). The HPLC system was composed of a vacuum degasser (type G1379A), a quaternary pump (type G1311A), an autosampler (type G1313A), and a diode-array detector (type G1315A). The detection wavelength was 210 nm. The separation column was an Eclipse XDB-C$_{18}$ (4.6 × 150 mm, 5 μm) with a mobile phase composed of methanol and 0.1 % phosphoric acid aqueous solution in a volume ratio of 90:10 at a flow rate of 1.0 mL·min^{-1}. The temperature of the column was 298.2 K.

RESULTS AND DISCUSSION

The solubility data of UA and OA in four solvents (methanol, ethanol, 2-propanol, and ethyl acetate) at various temperatures are presented in Tables 1 and 2, respectively (see also Figures 1 and 2). The solubilities of UA or OA as a function of temperature were correlated by the modified Apelblat equation (eq 1)[11−13]

$$\ln(x) = A + \frac{B}{T/\mathrm{K}} + C\ln(T/\mathrm{K}) \tag{1}$$

where x is the mole fraction solubility; T is the absolute temperature; and A, B, and C are the parameters of the equation. The parameters of A, B, and C were obtained by using a nonlinear regression and are presented in Table 3 or Table 4 together with the root-mean-square deviations (rmsd's) which are defined as eq 2.

$$\mathrm{rmsd} = \sqrt{\frac{\sum_{i=1}^{N}(x_i^c - x_i)^2}{N}} \tag{2}$$

Table 3. Parameters of eq 1 for UA in the Four Solvents

solvent	A	B	C	10^4 rmsd
methanol	−129.6002	4398.4607	20.1225	0.4068
ethanol	−128.8287	4333.3412	19.9831	0.5725
2-propanol	−68.9206	1675.7953	11.2038	0.9070
ethyl acetate	14.4522	−2893.7141	−0.8687	0.5030

Table 4. Parameters of eq 1 for OA in the Four Solvents

solvent	A	B	C	10^4 rmsd
methanol	−173.3726	6203.2834	26.6444	0.3668
ethanol	−160.5547	6170.1694	24.5426	0.9769
2-propanol	−176.8366	7144.6163	26.8323	1.1267
ethyl acetate	−159.4372	5502.6623	24.8652	0.5038

where N was the number of experimental points; x^c_i was the solubility calculated by eq 1; and x_i is the experimental value of mole fraction solubilities of UA or OA. The relative deviation is defined as eq 3.

$$\delta = |(x_i - x_i^c)/x_i| \tag{3}$$

where x_i was the experimental solubility and x^c_i was the solubility calculated from eq 1.

CONCLUSIONS

In this work, the solubilities of UA and OA in methanol, ethanol, 2-propanol, and ethyl acetate have been measured over the temperature range (283.2 to 329.7) K, and the calculated solubility shows good agreement with the experimental data. It has also been found that the solubilities of UA and OA in methanol, ethanol, 2-propanol, and ethyl acetate increase with increasing temperature. However, the solubilities of UA and OA are different in various solvents; the mole fraction solubility of UA in various solvents is in the order of: 2-propanol > ethyl acetate > methanol > ethanol, and the mole fraction solubility of OA in various solvents is in the order of: ethyl acetate > 2-propanol ≈ ethanol > methanol. Therefore, the measured solubility data and the correlation equation in this work can be applied to the design and optimization for the extraction and purification process of UA and OA.

AUTHOR INFORMATION

Corresponding Author

*Fax: +86 791 3969594. Tel.: +86 791 3969583. E-mail address: jasperfan@163.com.

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