Solubility of Oleanolic Acid in Various Solvents from (288.3 to 328.3) K

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The solubilities of oleanolic acid in ethanol, 1-butanol, acetone, and water were measured over the temperature range of (288.3 to 328.3) K. The experimental solubilities were fitted with the modified Apelblat equation.

Introduction

Oleanolic acid (3β-3-hydroxyolean-12-en-28-oic acid; CAS Registry Number 508-02-1; molecular weight 456.7; Figure 1) is a triterpenoid compound that exists widely in medicinal herbs and natural plants in the form of free acid or aglycones for triterpenoid saponins.[1,2] Oleanolic acid has many pharmaceutical functions, such as anti-inflammatory,[3,4] liver protection,[5] and enhancement of the body defense systems.[6]

Oleanolic acid has been isolated from more than 120 plant species.[7] It is usually extracted from these plants using organic solvents such as ethanol, 1-butanol, and acetone. Then oleanolic acid must be isolated from these solvents. Therefore, it is important to know the solubility data of oleanolic acid in these solvents and water.

In this study, the solubility of oleanolic acid in ethanol, 1-butanol, acetone, and water over the temperature range of (288.3 to 328.3) K was measured using HPLC, and the results were fitted with the modified Apelblat equation.

Experimental

Reagents and Apparatus. Oleanolic acid was obtained from Chengdu Jianjiang Pharmaceutical Factory (Sichuan, China). Ethanol (AR grade, 99.7 %+) was purchased from Shuanglin Chemical Reagent Factory (Hangzhou, Zhejiang). 1-Butanol (AR grade, 99.0 %+) and acetone (AR grade, 99.5 %+) were supplied by Gaojing Fine Chemical Co., Ltd. (Hangzhou, Zhejiang). Methanol (HPLC grade, 99.9 %+) was supplied by Tianjin Shield Company (Tianjin, China). HPLC grade water was used for the HPLC analysis. Other reagents used were of analytical grade. A THZ-C shaker was supplied by Jiangsu Taicang Laboratorial Equipment Factory, and the HPLC was purchased from Dionex Corporation

Sample Preparation. Excess amounts of oleanolic acid were added to 10 mL of various solvents (ethanol, 1-butanol, acetone, and water) at various temperatures from (288.3 to 328.3) K. The suspensions were shaken for 48 h in a shaker. After equilibria were attained, the supernatant liquid was withdrawn, filtered through a 0.45 μm membrane filter, appropriately diluted, and analyzed for oleanolic acid by HPLC.

Sample Analysis. The concentration of oleanolic acid was determined using a HPLC (Dionex Corporation, USA). The HPLC system consisted of a Dionex P 680A LPG-4 pump, a Dionex UVD-170U UV detector, a Dionex AST-100 automated sample injector, and a computer installed with Chromeleon version 6.60 software. The wavelength of detection was set at 210 nm. Separation was achieved using a Sepax HP-C18 (5 μm, 120 Å, 4.6 mm × 150 mm). The mobile phase consisted of CH_3OH, H_2O, and H_3PO_4 at a volume ratio of 95:5:0.01. The flow rate of the mobile phase was 1 mL·min^{-1}, and the injection volume was 50 μL. All chromatographic separations were performed at 25 °C. The calibration equation for oleanolic acid was established by using standard solutions in the concentration range of (0.5 to 40) μg·mL^{-1}. The recovery of oleanolic acid was evaluated to be (99.7 ± 0.9) %.

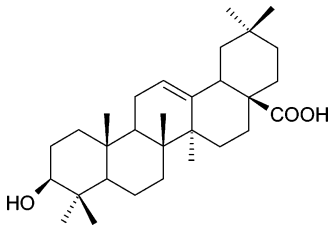

Figure 1. Chemical structure of oleanolic acid.

Results and Discussion

The solubility data of oleanolic acid in ethanol, 1-butanol, acetone, and water at various temperatures were measured and presented in Table 1. The solubility in 1-butanol was the highest, whereas that in water was the lowest. The solubility in ethanol, 1-butanol, acetone, and water increased with an increase in temperature. The solubility of oleanolic acid as a function of temperature was correlated by the modified Apelblat equation[8−11]

$$\ln(c/\text{mol}\cdot\text{L}^{-1}) = A + \frac{B}{T/\text{K}} + C\ln(T/\text{K}) \quad (1)$$

where c is the solubility of oleanolic acid; T is the absolute temperature; and A, B, and C are parameters. The parameters of A, B, and C were obtained using a nonlinear regression and are presented in Table 2 together with the root-mean-square deviations (rmsd's) which were defined as

$$\text{rmsd} = \sqrt{\frac{\sum_{i=1}^{N}(c_i^c - c_i)^2}{N}} \quad (2)$$

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Table 1. Solubility of Oleanolic Acid in Ethanol (1), 1-Butanol (2), Acetone (3), and Water (4)

T	c_1	$c_1 - c_1^c$	c_2	$c_2 - c_2^c$	c_3	$c_3 - c_3^c$	c_4	$c_4 - c_4^c$
K	10^2 mol·L^{-1}	10^2 mol·L^{-1}	10^2 mol·L^{-1}	10^2 mol·L^{-1}	10^2 mol·L^{-1}	10^2 mol·L^{-1}	10^5 mol·L^{-1}	10^5 mol·L^{-1}
288.3	0.89	−0.08	3.20	0.09	0.74	−0.14	0.48	−0.15
293.3	1.11	0.01	3.33	−0.06	1.12	0.06	0.85	0.07
298.3	1.35	0.09	3.82	0.10	1.37	0.10	1.08	0.14
303.3	1.49	0.07	3.97	−0.13	1.55	0.05	1.14	0.04
308.3	1.57	−0.04	4.41	−0.13	1.75	0.01	1.21	−0.06
313.3	1.71	−0.10	4.96	−0.10	1.96	−0.04	1.31	−0.11
318.3	2.11	0.07	5.90	0.25	2.20	−0.07	1.57	0.01
323.3	2.21	−0.08	6.47	0.14	2.54	−0.01	1.74	0.05
328.3	2.61	0.05	6.97	−0.15	2.87	0.04	1.78	−0.01

Table 2. Parameters of Equation 1 for Oleanolic Acid in the Solvents

solvent	A	B	C	rmsd
ethanol	−36.6	−477.6	5.94	$7.1 \cdot 10^{-4}$
1-butanol	−195.9	7142.9	29.61	$1.4 \cdot 10^{-3}$
acetone	212.6	−12259.8	−30.87	$6.9 \cdot 10^{-4}$
water	454.7	−23392.6	−68.06	$8.7 \cdot 10^{-7}$

where N was the number of experimental points; c_i^c represented the calculated solubility; and c_i represented the experimental solubility. The calculated solubilities of oleanolic acid were also given in Table 1. It could be seen that the calculated solubilities showed good agreement with the experimental values, which indicated that the modified Apelblat equation could be employed to correlate the measured solubility of oleanolic acid in the four solvents in the temperature range. The experimental solubility and the modified Apelblat equation with the parameters might be used as essential data for the study of oleanolic acid.

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