Solubility of Baicalin in Methanol, Ethanol, and Ethyl Acetate from (298.2 to 328.2) K

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The solubility of baicalin in methanol, ethyl acetate, and ethanol from (298.2 to 328.2) K was measured. The solubility of baicalin in these three solvents increases with increasing temperature. The solubility data were correlated with the Apelblat equation.

Introduction

Baicalin [$C_{21}H_{18}O_{11}$, CAS RN 21967-41-9, molecular weight 446.36], also named Baicalein 7-*O*-glucuronide (Figure 1), is one of the main bioactive flavone constituents in *Scutellaria baicalensis Georgi* with a wide range of beneficial activities.[1] It has been confirmed that baicalin has antibacterial, antiviral, and anti-inflammatory activities in vitro.[2−5] Baicalin also can inhibit platelet aggregation and eliminate oxygen-free radicals.[6,7] Animal experiments showed that baicalin could reduce the generation of endotoxin.[8] In addition, it has a potent effect in inhibiting pancreatin which is the initial metabolite of baicalin.

For pharmaceutical use, baicalin is usually extracted from the roots of *S. baicalensis Georgi* by using a base solution of water or organic solvents such as ethanol and methanol, followed by precipitation with acid solution. Now novel separation methods such as supercritical fluid extraction and microwave-assisted extraction have been reported.[9,10] However, crystallization from solution is still widely used to obtain a high purity product.[11] Therefore, it is important to determine the solubility data of baicalin in different solvents.

In this research, the solubility of baicalin in three common solvents, methanol, ethanol, and ethyl acetate, over the temperature range of (298.2 to 328.2) K was measured by ultraviolet spectrophotometry (UV).

Experimental Section

Reagents and Apparatus. Baicalin of pharmaceutical purity grade (≥ 99.0 %) was kindly donated by Shanghai Kaibao Pharmaceutical Co., Ltd. (Shanghai, China). All the reagents used such as ethanol and methanol were of analytical purity grade (99.5 %) and obtained from Dafang Chemical Reagent Factory (Hangzhou, China). Redistilled deionized water was used throughout.

The absorbance measurements of samples were carried out on a TU-1901 spectrophotometer (Puxi Tongyong Instrument Co. Ltd., China).

Sample Preparation. An excess amount of baicalin was added to the solvents in a specially designed sealed dual-wall flask. Between the outer and inner walls of the flask, water at constant temperature was circulated. The temperature was controlled by a thermostat (uncertainty of ± 0.1 K). The solution was constantly stirred using a magnetic stirrer. After the temperature was kept stable, the stirrer was turned off to let the solution settle for 2 h. Then the supernatant liquid was taken and filtered through a 0.45 μm membrane, and the samples were poured into a 50 mL volumetric flask and diluted to a fixed volume for UV analysis.

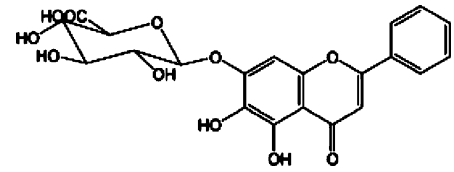

Figure 1. Molecular structure of baicalin.

Table 1. Solubility (c/mol·L^{-1}) of Baicalin in Methanol (1), Ethanol (2), and Ethyl Acetate (3) from (298.2 to 328.2) K

T/K	10^3c_1	$[(c_1 - c_1^{calcd})/c_1]$	10^3c_2	$[(c_2 - c_2^{calcd})/c_2]$	10^3c_3	$[(c_3 - c_3^{calcd})/c_3]$
298.2	3.157	−0.002	3.274	−0.007	0.110	−0.009
303.2	3.563	−0.006	3.357	0.026	0.151	0.006
308.2	3.862	0.005	3.485	0.007	0.201	0.045
313.2	4.125	−0.012	3.497	−0.047	0.225	−0.044
318.2	4.774	0.002	3.629	−0.018	0.269	−0.022
323.2	5.902	−0.000	3.680	0.105	0.324	0.046
328.2	6.152	−0.003	3.726	−0.049	0.332	−0.012

Sample Analysis. To determine the baicalin concentration in the solution, the absorbance of the standard and sample was measured at 272 nm because the maximum absorption wavelength of baicalin is $\lambda_{max} = 272$ nm. The calibration curve for baicalin was established by using the standard solutions in an appropriate concentration range of (3.20 to 32.0) mg·L^{-1}.

The saturated solubility of the solute (c) in three solvents was measured thrice. The relative uncertainty of the experimental solubility values is about 0.5 %.

Results and Discussion

The solubility values of baicalin in methanol, ethanol, and ethyl acetate were measured with their data shown in Table 1. The solubility of baicalin in methanol is the highest, whereas that in ethyl acetate is the lowest. The experimental data show that the solubility of baicalin in three solvents increases with increasing temperature.

The experimental solubility of baicalin increases with an increase in temperature. Thus the temperature dependence of

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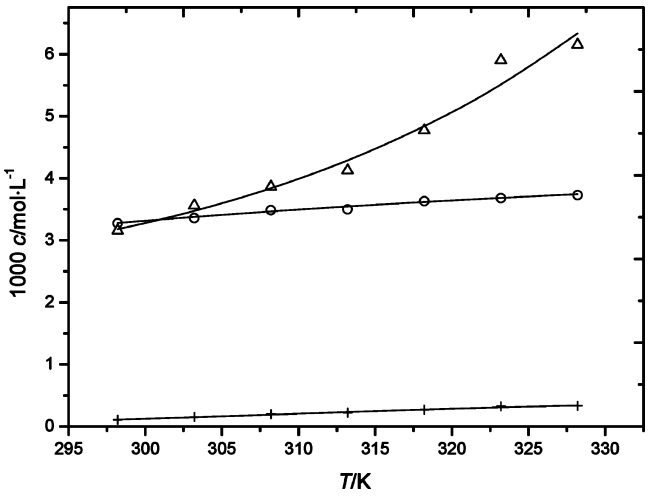

Figure 2. Solubility of baicalin in three solvents at different temperatures: Δ, methanol; ○, ethanol; +, ethyl acetate; −, calculated by eq 1.

Table 2. Parameters of Equations for Baicalin in the Three Solvents

solvent	*A*	*B*	*C*	10^4rmsd
methanol	−363.46	14682.2	54.139	1.79
ethanol	48.59	−2879.51	−7.837	0.23
ethyl acetate	998.4	−49745.27	−147.547	0.08

baicalin solubility in pure solvents can be correlated by the modified Apelblat equation.[12−14]

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

where c is the solubility of baicalin; T is the absolute temperature; and A, B, and C are the fitting parameters. The data of calculated solubility of baicalin are also shown in Table 1. The values of parameters A, B, and C and the root-mean-square deviations (rmsd) are listed in Table 2. The rmsd is defined as

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

where N is the number of experimental points and c_i^{calcd} and c_i represent the solubility calculated and the experimental solubility values, respectively. Figure 2 shows the calculated solubility of baicalin at different temperatures with the experimental values.

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