Solubility of Camellianin A in Methanol, Acetonitrile, Acetone, and Water from (283.2 to 313.2) K

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The solubility of camellianin A (4′,5,7-trihydroxyflavone; 5-*O*-[α-L-rhamnopyranosyl-(1→4)-6-*O*-acetyl-*β*-D-gluco-pyranoside]) in methanol, acetonitrile, acetone, and water from (283.2 to 313.2) K was measured under atmospheric pressure. The solubility of camellianin A in these solvents increases with increasing temperature. The solubility data were correlated with the Apelblat equation.

Introduction

Camellianin A (4′,5,7-trihydroxyflavone; 5-*O*-[α-L-rhamnopyranosyl-(1→4)-6-*O*-acetyl-*β*-D-glucopyranoside], CAS no. 109232-77-1; Figure 1), a naturally occurring flavone glycoside, largely exists with its content as high as 27.57 % ± 0.92 % in the leaves of *Adinandra nitida*, a famous folk tea in Guangxi province of P. R. China.[1] Previous pharmacological studies on this compound have demonstrated strong antioxidant activity[1,2] and significant anticancer effects against A431 tumor cells.[3] In addition, the flavonoid-rich methanol extract of the leaves of *A. nitida* showed remarkable 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity, at levels 10-fold higher than that of butylated hydroxytoluene.[4] As camellianin A exhibited antioxidant activity, it could be widely used in the food and pharmaceutical industry as a potential natural antioxidant and a functional ingredient as rutin.[2]

In our research, compared to silica gel or macroporous resin, crystallization is the most efficient and economical way to obtain pure camellianin A, in which solvents such as methanol, acetone, and so forth are frequently used. Therefore, the solubility data of camellianin A in different solvents is an important reference in the purification process studies.

In the present study, the solubilities of camellianin A in methanol, acetonitrile, acetone, and water over the temperature range of (283.2 to 313.2) K were measured, and the results were fitted with the modified Apelblat equation.

Experimental Section

Reagents and Apparatus. Camellianin A was isolated from the leaves of *A. nitida* by silica gel column chromatography. The minimum purity of camellianin A was higher than 99.0 % (the impurity in camellianin A was camellianin B, whose structure is very similar to camellianin A). After exhaustively recrystallization in methanol, the purity was ascertained by high-performance liquid chromatography (HPLC; Waters 2996 HPLC instrument coupled with a 2487 UV detector). The methanol, acetonitrile, and acetone (obtained from Shuanglin Chemical Reagent Factory, Hangzhou, China) were analytical purity grade. Deionized water was distilled before use. A THZ-C shaker was supplied by Taikang Laboratorial Equipment Factory (Henan, China). The absorbance measurements of samples were carried out on a TU-1901 spectrophotometer (Puxi Tongyong Instrument Co. Ltd., Beijing, China). The type of the cuvette is quartz, and the path length is 1 cm.

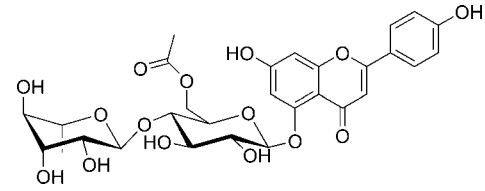

Figure 1. Molecular structure of camellianin A.

Sample Preparation. Excess amounts of camellianin A were added to 70 mL of the four solvents with their temperatures ranging from (283.2 to 313.2) K. The temperature was controlled by a thermostat (uncertainty of ± 0.1 K) in the shaker. The suspended solution was kept shaken for 24 h. After attaining equilibrium, the supernatant liquid was withdrawn and filtered through a 0.45 μm membrane. The filtered samples were diluted to an appropriate concentration for UV analysis. Each measurement was repeated three times. The measuring relative uncertainty of the experimental solubility values is ± 1 %.

Sample Analysis. To determine the concentration of camellianin A in the solution, the absorbance of the standard and the sample were measured at 329 nm, which is the maximum absorption wavelength of camellianin A. The calibration curve for the estimation of camellianin A was established by using the standard solutions in an appropriate concentration range.

Results and Discussion

The solubility values of camellianin A in methanol, acetonitrile, acetone, and water at different temperatures (camellianin A was thermal stability in the four solvents, monitored by HPLC) were measured with their data shown in Table 1. The solubility of camellianin A in different solvents is in the following order: methanol > water > acetonitrile > acetone. From the results, we found that the solubility of camellianin A increased with increasing polarity

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Table 1. Solubility (c) of Camellianin A in Water (1), Acetonitrile (2), Acetone (3), and Methanol (4) from (283.2 to 323.2) K[a]

T/K	$10^4\ c_1$	$(c_1 - c_1^{calc})/c_1$	$10^4\ c_2$	$(c_2 - c_2^{calc})/c_2$	$10^4\ c_3$	$(c_3 - c_3^{calc})/c_3$	$10^4\ c_4$	$(c_4 - c_4^{calc})/c_4$
283.2	0.948	0.007	0.427	−0.005	0.278	0.000	116.7	−0.006
293.2	1.308	−0.008	0.582	0.026	0.287	−0.014	162.8	0.022
298.2	1.567	−0.030	0.641	−0.025	0.302	0.003	181.7	0.009
303.2	1.899	0.038	0.747	−0.023	0.314	0.003	194.2	−0.030
308.2	2.326	0.010	0.925	0.037	0.327	−0.003	218.9	0.002
313.2	2.879	0.015	1.030	−0.014	0.345	−0.003	237.4	0.011

[a] The c_i,c_i^{calc} values are from the Apelblat parameters given in Table 2.

Table 2. Apelblat Parameter Equation Parameters for Camellianin A in the Four Solvents

solvent	A	B	C	10^5 rmsd
water	−427.34	15815.57	64.156	0.41
acetonitrile	−217.81	7019.79	32.405	0.19
acetone	195.35	7668.75	27.944	0.02
methanol	340.72	−17070.46	−50.457	30.8

of the solvents to some extent. The solubility of camellianin A in water (relative permittivity of 79.7,[5] 293.15 K) is higher than acetonitrile and acetone (relative permittivity of 37.5 and 20.6,[5] respectively, 293.15 K). However, the polarity of the solvent is not an absolute ingredient to determine the solubility, as the solubility in methanol (relative permittivity of 32.6,[5] 293.15 K) is obviously higher than water.

Corresponding to the empirical rule "like dissolves like", chemical structure also influences the solubility. It was hypothesized that the structure similarity between methanol and camellianin A due to the organic hydroxyl enhanced the solubility, and the addition of saccharides makes the whole glycoside molecule hydrophilicity, so the solubility of camellianin A is highest in methanol and lowest in acetone.

The experimental solubility of camellianin A increases with an increase in temperature. Thus the solubility of camellianin A as a function of temperature was fitted by the modified Apelblat equation.[6−10]

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

where A, B, C are the parameters; T is the absolute temperature, and c is the mole fraction solubility of camellianin A. The correlated values of A, B, and C of the four solvents and the root-mean-square deviations (rmsd) are listed in Table 2. The rmsd is defined as

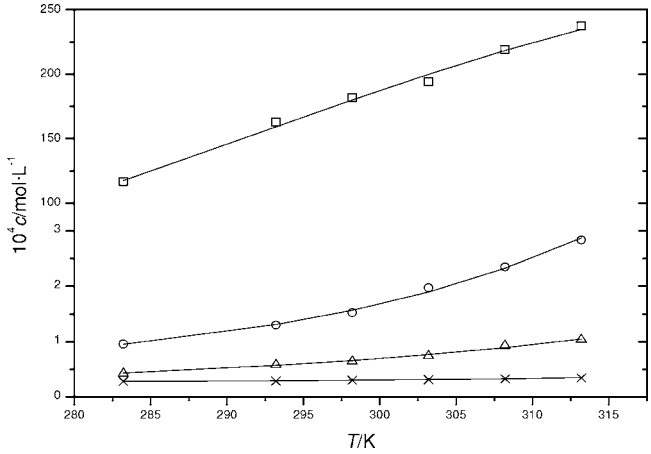

Figure 2. Solubility of camellianin A in different solvents at different temperatures: □, methanol; ○, water; Δ, acetonitrile; ×, acetone. The corresponding lines are from the calculated values by eq 1.

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

where N is the number of experimental points and c_i^{calc} and c_i represent the calculated and the experimental solubility values, respectively. The calculated solubility of camellianin A at different temperatures in four solvents (acetonitrile, acetone, water, and methanol) accords with the experimental data, which were also shown in Figure 2.

Conclusions

(1) The solubility of camellianin A in the four solvents (methanol, acetonitrile, acetone, and water) increased with the temperature increase.

(2) The solubility data calculated by the modified Apelblat equation are in good agreement with the experimental values.

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