Solubility of Hesperetin in Various Solvents from (288.2 to 323.2) K

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The solubilities of hesperetin in methanol, ethanol, 1-butanol, acetone, and water were measured over the temperature range of (288.2 to 323.2) K. The solubilities of hesperetin in selected solvents increased with an increase of temperature. The experimental solubilities were fitted with the modified Apelblat equation.

Introduction

Hesperetin (2*S*-2,3-dihydro-5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-4*H*-1- benzopyran-4-one; CAS Registry Number 520-33-2; molecular weight 302.3; Figure 1) is a flavonoid that exists widely in plants, fruits, flowers, and foods of plant origin.[1] As an important bioactive compound in medicinal herbs, hesperetin has biological and pharmacological activities, such as inhibition of cancer development,[2] anti-inflammatory,[3] antioxidant,[4] and lipid-lowering efficacy.[5]

Hesperetin is usually obtained from the hydrolysis of hesperidin.[6,7] Organic solvents and water must be applied in the process of separation and purification of hesperetin. Therefore, it is important to know the solubility of hesperetin in various solvents. Moreover, solubility is an important physicochemical parameter in the process of drug discovery and development.

In this study, the solubility of hesperetin in methanol, ethanol, 1-butanol, acetone, and water over the temperature range of (288.2 to 323.2) K was measured. The results were fitted with the modified Apelblat equation.

Experimental

Reagents and Apparatus. Hesperetin (98.0 %+) was obtained from Xiaocao Botanical Development Co., Ltd. (Shanxi, China). Methanol (AR grade, 99.5 %+) was purchased from Shanghai Chemical Reagent Co., Ltd. (Shanghai, China). Ethanol (AR grade, 99.7 %+) was supplied by Hangzhou Dafang Chemical Reagent Co., Ltd. (Zhejiang, China). 1-Butanol (AR grade, 99.0 %+) was supplied by Gaojing Fine Chemical Co., Ltd. (Zhejiang, China). Acetone (AR grade, 99.5 %+) was supplied by Hangzhou Chemical Reagent Co., Ltd. (Zhejiang, China). Deionized water was used throughout. A THZ-C shaker was supplied by Taicang Laboratorial Equipment Co., Ltd. (Jiangsu, China). A Spectrumlab 52 spectrophotometer was supplied by Lengguang Technology Co., Ltd. (Shanghai, China).

Sample Preparation. Excess amounts of hesperetin were added to 5 mL of various solvents (methanol, ethanol, 1-butanol, acetone, and water) at various temperatures from (288.2 to 323.2) K. The suspensions were shaken in a shaker for 22 h. After equilibrium was attained, the shaker was turned off to let the suspensions settle for 2 h.[8,9] The supernatant liquid was withdrawn, filtered with a 0.45 μm membrane filter, appropriately diluted, and analyzed for hesperetin using a UV spectrophotometer.

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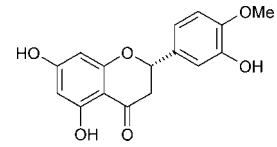

Figure 1. Chemical structure of hesperetin.

Sample Analysis. To determine the hesperetin concentration in solutions, the absorbance of the standards and samples was measured at 288 nm which is the maximum absorption wavelength of hesperetin as determined by us. The calibration equation for the determination of hesperetin was established by using standard solutions. The calibration equation was set as $Y = 0.0205X + 0.0028$ and $R^2 = 0.9998$ in the concentration range of ($5.69 \cdot 10^{-6}$ to $3.41 \cdot 10^{-5}$) mol·L^{-1}, where Y was UV absorbance and X was concentration of standard solutions.

Results and Discussion

Twenty-four hours was decided as the incubation time (shaking time plus 2 h of sedimentation time) for the measurement of solubility of hesperetin based on a preliminary experiment. The solubilities of hesperetin in all selected solvents at different temperatures were measured and presented in Table 1. The solubility in acetone was the highest, whereas that in water was the lowest. The solubility in all selected solvents increased with an increase of temperature in the range of (288.2 to 323.2) K.

The solubility of hesperetin as a function of temperature was fitted by the modified Apelblat equation[10,11]

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

where c is the solubility of hesperetin; 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 were presented in Table 2 together with the root-mean-square deviation (rmsd) which is defined as

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

where N is the number of experimental points; c_i^{c} represents the solubility calculated; and c_i represents the experimental solubility. It could be seen that the calculated solubilities showed good agreement with the experimental values from the small

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Table 1. Solubility of Hesperetin in Methanol (1), Ethanol (2), 1-Butanol (3), Acetone (4), and Water (5)

T	c_1	c_2	c_3	c_4	c_5
K	10^{-1} mol·L^{-1}	10^{-1} mol·L^{-1}	10^{-2} mol·L^{-1}	10^{-1} mol·L^{-1}	10^{-5} mol·L^{-1}
288.2	0.85 ± 0.00	0.69 ± 0.01	3.01 ± 0.03	2.85 ± 0.04	0.12 ± 0.01
293.2	0.92 ± 0.02	0.73 ± 0.01	3.20 ± 0.05	3.12 ± 0.05	0.24 ± 0.01
298.2	1.06 ± 0.02	0.87 ± 0.02	3.70 ± 0.06	3.40 ± 0.01	0.45 ± 0.01
303.2	1.11 ± 0.01	0.93 ± 0.02	4.19 ± 0.06	3.66 ± 0.05	0.86 ± 0.02
308.2	1.27 ± 0.03	1.07 ± 0.02	4.68 ± 0.03	3.83 ± 0.05	1.71 ± 0.01
313.2	1.42 ± 0.01	1.16 ± 0.03	5.39 ± 0.07	3.85 ± 0.07	3.30 ± 0.03
318.2	1.62 ± 0.01	1.31 ± 0.01	6.41 ± 0.08	3.94 ± 0.06	5.88 ± 0.04
323.2	1.87 ± 0.02	1.32 ± 0.02	7.19 ± 0.10	4.29 ± 0.04	11.23 ± 0.06

Table 2. Parameters of Equation 1 for Hesperetin in the Selected Solvents

solvent	*A*	*B*	*C*	rmsd
methanol	− 318.7	12606.5	48.11	$3.3 \cdot 10^{-3}$
ethanol	198.9	− 10748.3	− 29.01	$3.5 \cdot 10^{-3}$
1-butanol	− 271.5	10141.6	41.10	$9.2 \cdot 10^{-4}$
acetone	200.7	− 9995.1	− 29.53	$9.5 \cdot 10^{-3}$
water	− 466.9	10652.4	73.53	$1.6 \cdot 10^{-6}$

rmsd, which indicated that the modified Apelblat equation could be employed to fit the measured solubility of hesperetin in the selected five solvents in the temperature range. The experimental solubility and parameters of the modified Apelblat equation might be used as important fundamental data for the separation, purification, and pharmaceutical research of hesperetin.

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Supporting Information Available:

Tables 3 and 4. This material is available free of charge via the Internet at http://pubs.acs.org.

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