Solubility of Physalin D in Ethanol, Methanol, Propanone, Trichloromethane, Ethyl Ethanoate, and Water at Temperatures from (283.2 to 313.2) K

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The solubility of physalin D in ethanol, methanol, propanone, trichloromethane, ethyl ethanoate, and water at temperatures from (283.2 to 313.2) K was measured under at a pressure of 0.1 MPa. The solubility of physalin D in these solvents increases with increasing temperature. The experimental solubility data were correlated with the Apelblat equation.

Introduction

Physalin D (17,3-(epoxymethano)-1,17:2,6-dimethano-17*H*-naphtho[1,2-*f*]furo[3,4-*b*:2,3-*c*′]bisoxocin-4,8,11,21(1*H*,8a*H*,10*bH*)-tetrone,2,3,6,6*a*,9,10,10*a*,14,14*a*,15,16,16*a*-dodecahydro-8*a*,14*a*,15-trihydroxy-2,6*a*,10*b*-trimethyl-(1*S*,2*S*,3*S*,6*R*,6a*S*,8a*R*,10a*S*,10b*R*,14a*R*,15*R*,16a*R*,17*R*,18a*R*); CAS Registry No. 54980-22-2; $C_{28}H_{32}O_{11}$; molecular mass 544.55 g·mol^{-1}; shown in Figure 1) is a steroid that exists widely in stems, leaves, and fruit calyxes of plants *Physalis angulata*,[1,2] *Physalis solanaceus*,[3] and *Physalis alkekengi var. franchetii*.[4] As an important bioactive compound in these important herb medicines, physalin D has many biological and pharmacological activities, such as antimycobacterial,[2] antitumor,[5] immune depression,[6] and cytotoxic activity.[1,7,8]

In previous studies, physalin D and other physalins were often extracted by water, methanol, or ethanol, partitioned with trichloromethane, and then purified through silica gel or macroporous resin column,[1,2] but in our research, we found that, compared to column chromatography, crystallization in propanone was the most efficient and economical way to obtain pure physalin D. Therefore, the solubility data of physalin D in these solvents are important references in the extraction and purification process studies. Moreover, solubility is also an important physicochemical parameter in the process of structure modification and pharmaceutical preparations.

In this study, the solubility of physalin D in six common solvents, including ethanol, methanol, propanone, trichloromethane, ethyl ethanoate, and water, over the temperature range of (283.2 to 313.2) K was measured by high-performance liquid chromatography (HPLC), and the results were fitted with the modified Apelblat equation.

Experimental Section

Reagents and Apparatus. Physalin D was isolated from the aerial parts of *P. angulata* by silica gel column chromatography and recrystallization in propanone. The minimum mole fraction purity of physalin D was higher than 0.99, and the purity was ascertained by HPLC. The ethanol, methanol, propanone, trichloromethane, and ethyl ethanoate (obtained from Shuanglin Chemical Reagent Factory, Hangzhou, China) used for dissolving were analytical purity grade with a mass fraction purity > 0.99, and deionized water was distilled before using; methanol (Merck, Darmstadt, Germany) used for the mobile phase was of HPLC grade with a mass fraction purity > 0.99. A DFY-5/40 bath cryostat, which could control the temperature precisely from (268.2 to 313.2) K, was supplied by Gongyi City Jinghua Instrument Company (Henan, China). An Aglient 1200 HPLC instrument coupled with a G1315C DAD detector was used for the analysis of samples.

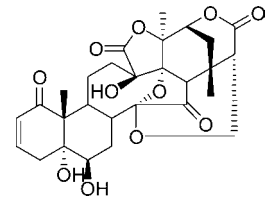

Figure 1. Molecular structure of physalin D.

Sample Preparation. Excess amounts of physalin D were added to 10 cm^3 of the six 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 bath cryostat. The suspended solution was kept stirred by magnetic stirrer 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 HPLC analysis. Triplicate samples were prepared for each data point.

Sample Analysis. To determine the concentration of physalin D, the HPLC system mentioned above was used with its wavelength of detection set at 230 nm. All chromatographic separations were performed using an Agilent ZORBAX SB-C18 column (250 mm × 4.60 mm, 0.05 mm). The mobile phase was methanol (1) + water (2) with a volume fraction of 0.5 and flow rate at 0.017 cm^3·s^{-1}, the injection volume being 0.02 cm^3. The calibration curve for estimation of physalin D was established by using the standard solutions in the appropriate concentration range.

Results and Discussion

The solubility values of physalin D in ethanol, methanol, propanone, trichloromethane, ethyl ethanoate, and water at different temperatures were measured with their data shown in Table 1. The solubility of physalin D in different solvents is in the following order: (1) for temperatures between (283.2 and 293.2) K: propanone > methanol > trichloromethane > ethanol

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Table 1. Solubility c of Physalin D in Ethanol (1), Methanol (2), Propanone (3), Ethyl Ethanoate (4), Water (5), and Trichloromethane (6) at Temperature T

T/K	$10^2\,c_1$/mol·dm^3	$\{c_1 - c_1(\text{calc})\}/c_1$	$10^2\,c_2$/mol·dm^3	$\{c_2 - c_2(\text{calc})\}/c_2$	$10^2\,c_3$/mol·dm^3	$\{c_3 - c_3(\text{calc})\}/c_3$	$10^2\,c_4$/mol·dm^3	$\{c_4 - c_4(\text{calc})\}/c_4$	$10^2\,c_5$/mol·dm^3	$\{c_5 - c_5(\text{calc})\}/c_5$	$10^2\,c_6$/mol·dm^3	$\{c_6 - c_6(\text{calc})\}/c_6$
283.2	0.39	0.020	0.81	−0.019	1.73	−0.001	0.30	−0.009	0.12	−0.035	0.46	−0.004
293.2	0.47	−0.035	0.92	0.024	2.20	0.012	0.32	−0.026	0.21	−0.088	0.47	−0.014
298.2	0.58	0.011	1.01	0.015	2.38	−0.011	0.36	−0.032	0.27	0.015	0.49	−0.029
303.2	0.71	0.026	1.09	−0.024	2.65	0.004	0.42	−0.004	0.28	−0.046	0.53	−0.002
308.2	0.89	0.036	1.22	−0.064	2.86	−0.001	0.52	−0.027	0.29	−0.068	0.58	0.027
313.2	1.07	−0.020	1.59	0.035	3.09	0.003	0.59	−0.040	0.30	−0.031	0.60	−0.031

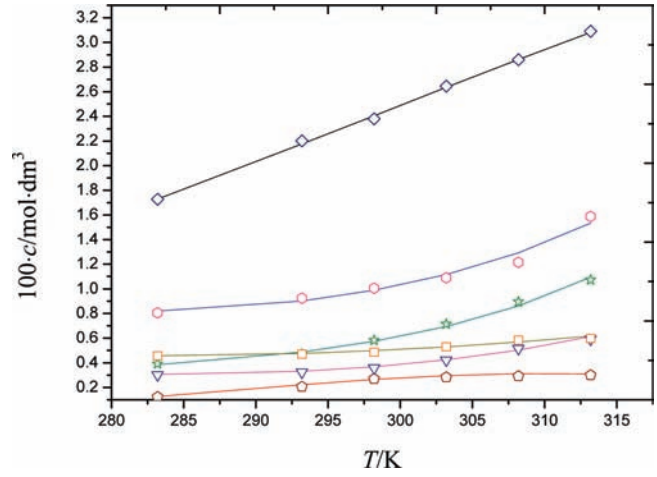

Figure 2. Solubility c of physalin D in different solvents at temperatures T: ◇, propanone; ○, methanol; ☆, ethanol; □, trichloromethane; ▽, ethyl ethanoate; ⬠, water. The corresponding lines are calculated from eq 1.

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

solvent	A	B	C	10^4 rmsd
ethanol	−775.249	31600	116.558	1.91
methanol	−743.576	31280	111.283	4.23
propanone	142.369	−7950	−20.962	1.60
ethyl ethanoate	−938.669	39710	140.388	1.26
water	1423	−65770	−212.079	1.29
trichloromethane	−317.600	15530	55.148	1.18

> ethyl ethanoate > water; and (2) for temperatures between (293.2 and 313.2) K: propanone > methanol > ethanol > trichloromethane > ethyl ethanoate > water, as shown in Figure 2. These experimental data could be regressed by eq 1 for each solvent. Among these solvents, the solubility of physalin D in propanone increased most significantly with the increasing temperature. The result suggested that the polarity of the solvent is not the only factor to determine the solubility, as the solvents' polarity is in the following order: water > methanol > ethanol > propanone > ethyl ethanoate > trichloromethane. It was hypothesized that the structure similarity between the solvent and the solute due to the ketone group enhanced the solubility significantly, corresponding to the empirical rule "like dissolves like" to some extent; moreover, being able to form hydrogen bonds (—OH in the drug with ═O in propanone) may also help to increase the solubility of physalin D.

The experimental solubility of physalin D increases with an increase in temperature (Figure 2). Thus the solubility of physalin D as a function of temperature was fitted by the modified Apelblat equation[9−12]

$$\ln(c/\text{mol}\cdot\text{dm}^3) = A + B/(T/\text{K}) + C\ln(T/\text{K}) \qquad (1)$$

where A, B, and C are the parameters, T is the temperature, and c is the molarity solubility of physalin D. The correlated values of A, B, and C of the six solvents and the root-mean-square deviations (rmsd's) are listed in Table 2.

The rmsd is defined as

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

where N is the number of experimental points and c_i(calc) and c_i represent the calculated and the experimental solubility values, respectively. From Tables 1 and 2, it could be seen that the

calculated solubilities show good agreement with the experimental values, which suggested that the modified Apelblat equation can be employed to fit the measured solubility of physalin D in the selected six solvents and the temperature range.

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