Solubility of Gallic Acid in Methanol, Ethanol, Water, and Ethyl Acetate

Ali Daneshfar,*,[†] Hassan S. Ghaziaskar,[‡] and Nasrolah Homayoun[†]

Department of Chemistry, Faculty of Science, Ilam University, Ilam, 69315516, Iran, and Department of Chemistry, Isfahan University of Technology, Isfahan, 8415683111, Iran

The solubility of gallic acid in methanol, ethanol, water, and ethyl acetate was measured at a temperature range of (298.2 to 333.2) K. The gallic acid solubility in different solvents increases smoothly with temperature. The relative solubility of gallic acid in the solvents was found as: $w_{\text{methanol}} > w_{\text{ethanol}} > w_{\text{water}} > w_{\text{ethyl acetate}}$. The temperature dependence of the solubility data was correlated by the modified Apelblat model. The calculated solubilities show good agreement with the experimental data in the temperature range studied.

Introduction

Gallic acid (3,5,7-trihydroxybenzoic acid) and its derivative are natural products of hydrolysis of tannins.[1] They are present in plants, such as green and black teas,[2] pomegranate husk,[3] oak,[4] and grape.[5] Since they were found to have many significant biological activities, such as antioxidant,[6] antiinflammatory,[7] antifungal,[5] and carcinogenic[1] properties, they have attracted considerable interest. Gallic acid and its esters are industrially important chemicals used in the food and pharmaceutical industry (synthesis of propyl gallate and trimethoprim).[3,8] The aqueous solubility of organic compounds plays an important role in their industrial, pharmaceutical, separation, purification, and environmental applications.[9,10] To determine proper solvents and to design an optimized production process, it is necessary to know the solubility of gallic acid in different solvents.

In this work, gallic acid solubility in water, ethyl acetate, ethanol, and methanol over a temperature range of (298.2 to 333.2) K was measured by a static method. To the best of our knowledge, the solubility of gallic acid in ethyl acetate, ethanol, and methanol has not been previously reported, and the results can be used in the extraction and purification of gallic acid from different matrices.

Experimental Section

Materials. Gallic acid monohydrate, with a purity of 99.5 mass %, was purchased from Scharlau (Barcelona, Spain). Gallic acid was dried to constant weight in an air oven at 383 K before use. Ethanol, ethyl acetate, and methanol were supplied by Merck Chemical Co. (Germany), and doubly distilled water was used for all the experiments. All the chemicals were of analytical reagent grade.

Apparatus and Procedure. Saturated solutions of gallic acid in each solvent were prepared in a spherical, 50 mL Pyrex glass flask. The flask was maintained at the desired temperature through circulating water. The water temperature was controlled by a thermostat within ± 0.1 K that was provided from a constant-temperature water bath. For each measurement, an excess amount of gallic acid was added to a known volume of solvent (20 mL). The solution was constantly stirred using a Teflon-coated magnetic stirring bar running at (400 to 500) rpm and allowed to mix for 4 h. Then, the solution was allowed to settle at least 1 h before sampling. The upper portion was taken, filtered, and poured into a volumetric flask, weighed, and diluted with the neat solvent. The prepared sample was finally analyzed by a UV/vis spectrophotometric method at (269, 269.5, 273, and 273) nm for water, ethyl acetate, methanol, and ethanol solvents, respectively. A CECIL UV/vis spectrophotometer (model 3000, UK) was used for the concentration measurements. Since the solutes were in a pure form, the UV/vis spectrophotometric method was used for the concentration determination.

The external calibration curve was used for quantitation of gallic acid in different solvents. The solubility was expressed as mass fraction and calculated as gram of solute to the sum of grams of solute and solvent. To extend the measurements to other temperatures, the experimental solubilities were fitted to the Apelblat proposed equation, and the parameters of the model were calculated. This model was found to be the best among different proposed models. Each data reported is at least an average of three measurements at each condition.

Results and Discussion

To validate the method of solubility measurement, the solubility of gallic acid in pure water was determined at the temperature range of (303 to 333) K. As shown in Figure 1, the solubilities are similar with respect to the values reported in the literature.[8] The difference observed between our result and the results reported in ref 8 is mostly due to the difference in methods of analysis or experimental error. The concentrations of gallic acid have been measured by reverse-phase high-performance liquid chromatography, and UV–vis spectrophotometry has been used to determine the solubility in this work.

The solubility of sodium chloride in water at the temperature range of (303 to 356) K was also measured using the method used as shown in Figure 2. These data also validate the data reported in comparison with the previously reported data.[11] The uncertainty of results for at least three measurements was found to be better than 0.33 %.

---

* Corresponding author. Telfax: +98-841-2227022. E-mail: daneshfara@yahoo.com.

[†] Ilam University.

[‡] Isfahan University of Technology.

10.1021/je700633w CCC: $40.75

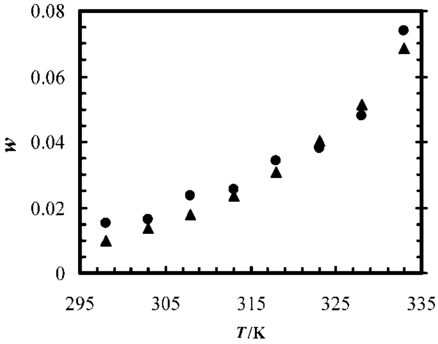

Figure 1. Mass fraction solubility of gallic acid in water at different temperatures: •, this work; ▲, literature values.[8]

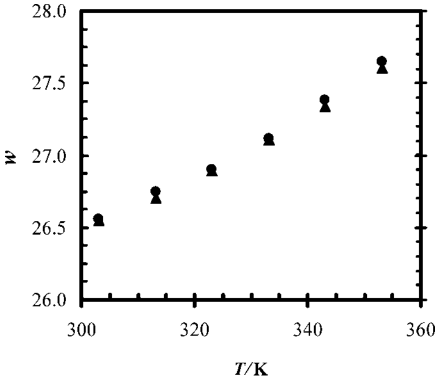

Figure 2. Mass fraction solubility of sodium chloride in water at different temperatures: •, this work; ▲, literature values.[11]

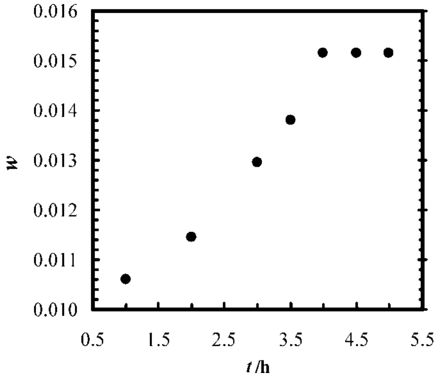

Figure 3. Mass fraction solubility of gallic acid in water at 298.2 K as a function of time.

Table 1. Experimental (w) and Calculated (w_{calcd}) Mass Fraction Solubility of Gallic Acid in Methanol, Ethanol, Water, and Ethyl Acetate from T = (298.2 to 333.2) K

T/K	100 (w ± SD[a])	100 w_{calcd}
	Methanol	
298.2	27.93 ± 0.29	28.11
303.2	28.83 ± 0.29	28.63
308.2	29.30 ± 0.30	29.15
313.2	29.59 ± 0.30	29.66
318.2	30.13 ± 0.30	30.16
323.2	30.48 ± 0.32	30.65
328.2	31.07 ± 0.33	31.13
333.2	31.74 ± 0.33	31.61
	Ethanol	
298.2	18.90 ± 0.22	18.84
303.2	18.94 ± 0.21	18.96
308.2	19.00 ± 0.22	18.98
313.2	19.17 ± 0.23	19.19
318.2	19.55 ± 0.24	19.49
323.2	20.02 ± 0.24	19.88
328.2	20.45 ± 0.24	20.36
333.2	20.93 ± 0.25	20.93
	Water	
298.2	1.516 ± 0.021	1.505
303.2	1.615 ± 0.021	1.760
308.2	2.367 ± 0.021	2.117
313.2	2.540 ± 0.023	2.580
318.2	3.429 ± 0.026	3.210
323.2	3.820 ± 0.026	4.071
328.2	4.787 ± 0.026	5.230
333.2	7.378 ± 0.037	6.831
	Ethyl Acetate	
298.2	1.276 ± 0.020	1.274
303.2	1.290 ± 0.021	1.281
308.2	1.303 ± 0.020	1.310
313.2	1.335 ± 0.021	1.360
318.2	1.438 ± 0.023	1.429
323.2	1.544 ± 0.023	1.509
328.2	1.598 ± 0.024	1.595
333.2	1.689 ± 0.024	1.703

[a] Standard deviations (SD) are based on at least three measurements at each temperature.

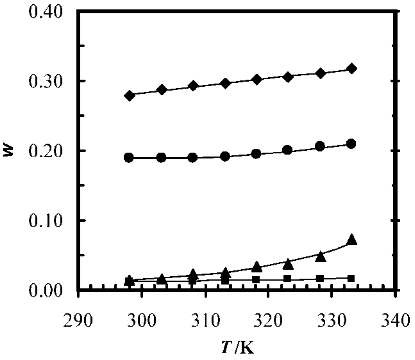

Figure 4. Mass fraction solubility of gallic acid in different solvents as a function of temperature: ♦, methanol; •, ethanol; ▲, water; ■, ethyl acetate; −, correlated data.

To find the equilibrium condition, the dissolution was measured at different times. As shown in Figure 3, the dissolution of gallic acid in water as a function of time increases until it reaches a plateau after (4 to 5) h at 298.2 K where the solubility can be measured. Constant and reproducible solubility data after 4 h were taken as an indication of reaching equilibrium conditions.

The experimental and calculated mass fraction solubility data of gallic acid in methanol, ethanol, water, and ethyl acetate at different temperatures are listed in Table 1 and shown graphically in Figure 4. The experimental data show that the solubility of gallic acid in different solvents increases smoothly with increasing temperature. However, the solubility of gallic acid in methanol is higher than in ethanol, water, and ethyl acetate. On the basis of the solubility data, it can be observed that the highest solubilities were obtained in pure methanol and the lowest values were found in pure ethyl acetate. Very small standard deviations of measurements indicate that the system is in saturation conditions.

The temperature dependence of gallic acid solubility in methanol, ethanol, water, and ethyl acetate can be well-correlated by the modified Apelblat equations[12–15]

$$\ln(w) = A + B/(T/\text{K}) + C\ln(T/\text{K}) \qquad (1)$$

in which w is the mass fraction solubility of gallic acid and T is the absolute temperature. The parameters A, B, and C were obtained by fitting the experimental solubility data and are

Table 2. Apelblat Equation Parameters *A*, *B*, and *C* for Correlation of Gallic Acid Data in Different Solvents at T = (298.2 to 333.2) K

solvent	A	B	C	$10^2\sigma^a$
methanol	0.367	−356.973	−0.077	0.0086
ethanol	−131.597	5807.949	19.385	0.1472
water	−652.297	26603.384	98.089	0.0518
ethyl acetate	−282.717	12277.939	41.626	0.00817

[a] σ = the root-mean-square deviation.

presented in Table 2 together with the root-mean-square deviations. The rmsd is defined as

$$\sigma = \left[\frac{1}{n}\sum_{i=1}^{n}(w_i^{\text{calcd}} - w_i)^2\right]^{1/2} \qquad (2)$$

where n is the number of experimental values and w_i^{calcd} and w_i represent the calculated and the experimental mass fraction solubility values, respectively. As shown in Table 2 and Figure 4, the experimental values are correlated very well with the calculated solubilities.

Conclusions

The solubilities of gallic acid in methanol, ethanol, water, and ethyl acetate were measured at temperatures from (298.2 to 333.2) K. Raising the temperature increased the solubility of gallic acid regardless of the solvent used. The solubility data show that the trend of solubility in different solvent is: $w_{\text{methanol}} > w_{\text{ethanol}} > w_{\text{water}} > w_{\text{ethyl acetate}}$. The temperature dependence of gallic acid solubility in different solvents can be well-correlated by the modified Apelblat equations, and the calculated solubilities show good agreement with the experimental values.

Literature Cited

(1) Mammela, P.; Tuomainen, A.; Savolainen, H.; Kangas, J.; Vartiainen, T.; Lindroos, L. Determination of Gallic Acid in Wood Dust as an Indicator of Oak Content. *J. Environ. Monit.* **2001**, *3*, 509–511.
(2) Zuo, Y.; Chen, H.; Deng, Y. Simultaneous Determination of Catechins, Caffeins and Gallic Acid in Green, Oolong, Black and Pu-erh Teas Using HPLC with a Photodiode Array Detector. *Talanta* **2002**, *57*, 307–316.
(3) Lu, J. J.; Wei, Y.; Yuan, Q. P. Preparative Separation of Gallic Acid from Chinese Traditional Medicine by High-Speed Counter-Current Chromatography and Followed by Preparative Liquid Chromatography. *Sep. Purif. Technol.* **2007**, *55*, 40–43.
(4) Mammela, P.; Savolainen, H.; Lindroos, L.; Kangas, J.; Vartiainen, T. Analysis of Oak Tannins by Liquid Chromatography–Electrospray Ionisation Mass Spectrometry. *J. Chromatogr. A.* **2000**, *891*, 75–83.
(5) Yilmaz, Y.; Toledo, R. T. Major Flavonoids in Grape Seeds and Skins: Antioxidant Capacity of Catechin, and Gallic Acid. *J. Agric. Food Chem.* **2004**, *52*, 255–260.
(6) Alberto, M. R.; Farias, M. E.; Manca de Nadra, M. C. Effect of Gallic Acid and Catechin on Lactobacillus Hilgardii 5w Growth and Metabolism of Organic Compounds. *J. Agric. Food Chem.* **2001**, *49*, 4359–4363.
(7) Chafer, A.; Fornari, T.; Stateva, R. P.; Berna, A.; Reverter, J. G. Solubility of the Natural Antioxidant Gallic Acid in Supercritical CO_2+Ethanol as a Cosolvent. *J. Chem. Eng. Data* **2007**, *52*, 116–121.
(8) Lu, L. L.; Lu, X. Y. Solubilities of Gallic Acid and Its Esters in Water. *J. Chem. Eng. Data* **2007**, *52*, 37–39.
(9) Ran, Y.; He, Y.; Yang, G.; Johnson, J. L. H.; Yalkowsky, S. H. Estimation of Aqueous Solubility of Organic Compounds by Using the General Solubility Equation. *Chemosphere* **2002**, *48*, 487–509.
(10) Lu, J.; Wang, X. J.; Yang, X.; Ching, C. B. Solubilities of Glycine and Its Oligopeptides in Aqueous Solutions. *J. Chem. Eng. Data* **2006**, *51*, 1593–1596.
(11) Pinho, S. P.; Marcedo, E. A. Solubility of NaCl, NaBr, and KCl in Water, Methanol, Ethanol, and Their Mixed Solvents. *J. Chem. Eng. Data* **2005**, *50*, 29–32.
(12) Zou, Z.; Dang, L.; Liu, P.; Wei, H. Solubility of Fluorene in Different Solvents from (278.98 to 338.35) K. *J. Chem. Eng. Data* **2007**, *52*, 1501–1502.
(13) Yang, Z. J.; Hu, H. B.; Zhang, X. H.; Xu, Y. Q. Solubility of Phenazine-1-Carboxylic Acid in Water, Methanol, and Ethanol from (278.2 to 328.2) K. *J. Chem. Eng. Data* **2007**, *52*, 184–185.
(14) Hao, H. X.; Wang, J. K.; Wang, Y. L. Solubility of Dexamethasone Sodium Phosphate in Different Solvents. *J. Chem. Eng. Data* **2004**, *49*, 1697–1698.
(15) Wang, L. H.; Cheng, Y. Y. Solubility of Puerarin in Water, Ethanol, and Acetone from (288.2 to 328.2) K. *J. Chem. Eng. Data* **2005**, *50*, 1375–1376.

Received for review October 31, 2007. Accepted January 19, 2008. The authors thank the research council of Ilam University for financial support.

JE700633W