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Experimental measurement and correlation of the solubility of aloe-emodin in seven pure solvents

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ABSTRACT

The solubility of aloe-emodin in seven pure solvents namely water, methanol, ethanol, 1-propanol, 1-butanol, 2-butanol, and 1-pentanol was measured by a static analytic method. The measurements were carried out over the temperature range from (278.15 to 318.15) K at 5 K intervals under atmospheric pressure using a UV/vis spectrophotometer analysis. The effects of experimental temperature and solvent type on the solubility are discussed. The relative solubility of aloe-emodin in seven solvents was determined in elevated order to be $x_{water} < x_{methanol} < x_{ethanol} < x_{2\text{-butanol}} < x_{1\text{-propanol}} < x_{1\text{-butanol}} < x_{1\text{-pentanol}}$. The experimental result shows that 1-pentanol could be a suitable solvent for industrial preparation of aloe-emodin. The experimental solubility values were correlated with the modified Apelblat and λh models. It was found that the two empirical thermodynamic models can satisfactorily correlate the solubility of aloe-emodin in the seven solvents over the range of temperature studied.

1. Introduction

Aloe-emodin (1,8-dihydroxy-3-(hydroxymethyl)-9,10-anthracenedione, AE) is a bioactive anthraquinone naturally present in the leaves of *Aloe vera* and other species of the *asphodelaceae* and the *polygonaceae* families [1,2]. The chemical structure of aloe-emodin is shown in figure 1. This compound has recently been demonstrated to have various pharmacological activities, such as laxative, antibacterial, and hepatoprotective activities [3–6], and recently it was found to exert a potent anticancer and immunomodulatory activity on BRAF-mutated human melanoma cells through GM-CSF and IFN-γ production [7–10].

Due to its prophylactic and therapeutic properties, aloe-emodin has received great attention. However, aloe-emodin is almost insoluble in water and is obtained mainly from plant materials by extraction with different organic solvents or their mixtures or ionic liquids [11–13]. In the herbal extracts, aloe-emodin always coexists with other anthraquinone derivatives, including emodin, aloe-emodin, chrysophanol, and physcion. For these biological and pharmaceutical products, some purified methods such as high-speed counter current chromatography (HSCCC), high performance liquid chromatography (HPLC), thin-layer chromatography (TLC) have been developed [14]. All these separation processes involve the use of organic solvents. In order to select a proper solvent for these separation processes, the solubility in various solvents and temperature range is obviously one of the most important properties that can be quantitatively determined [15–19]. The temperature dependent solubility of aloe-emodin in water and borax-sodium carbonate buffers has been reported by Stone and Furman [11]. Li *et al.* have measured the solubility of aloe-emodin with cyclodextrin and its derivatives through inclusion action by phase solubility method [12]. The solubility of aloe-emodin in five imidazolium-based ionic liquids has also been measured by several researchers [13]. Their results show that IL $[C_4mim]NTF_2$ exhibited good dissolubility to aloe-emodin. However, to the best of our knowledge, the temperature dependent solubility of aloe-emodin in methanol, ethanol, 1-propanol, 1-butanol, 2-butanol, and 1-pentanol solvents have not been systematically reported in the litreature. The modified Apelblat [20–22] and λh [17–23] models are the commonly used mathematical models to correlate the experimental solubility values with experimental solubility values.

In this work, we measured the solubility of aloe-emodin in water, methanol, ethanol, 1-propanol, 1-butanol, 2-butanol, and 1-pentanol over the temperature range from (278.15 to 318.15) K at atmospheric pressure of 0.1 MPa. Then the experimental values were correlated with the modified Apelblat equation and λh equation. Comparison and discussion of the solubility were carried out. In addition, the thermodynamic properties of the system, such as

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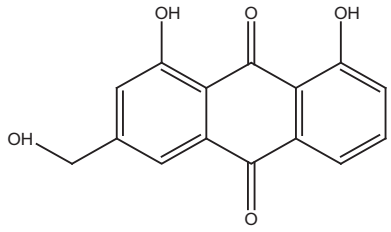

FIGURE 1. Chemical structure of aloe-emodin.

the dissolution enthalpy, entropy, and molar Gibbs energy were also determined using the van't Hoff equation. The aloe-emodin solubility data of this work could be useful in purification, crystallization and separation in chemical or pharmaceutical industries.

2. Experimental

2.1. Materials

Aloe-emodin (mass fraction purity > 0.980) was supplied by Shanghai Yuanye Bio-technology Co. Ltd, (Shanghai, China). Methanol and ethanol were purchased from Sinopharm Chemical Reagent Co. Ltd., (Beijing, China). The 1-propanol, 1-butanol, and 1-pentanol were purchased from Tianjin Kermel Chemical Reagent Factory (Tianjing, China); 2-butanol was supplied by Tianjin Guangcheng Chemical Reagent Co. Ltd., (Beijing, China). The water used in this work was high pure chromatographic grade water which was obtained from Elga Purelab water system (Elga, England) and the conductivity of water is <1 μS·cm^{-1}. All the materials in this work were used without any further purification. The solvent polarity is a useful parameter to evaluate the influence of a solvent to dissolve a specific solute. The normalized E_T^N value adopted from the litreature has been introduced to explain the solubility value of aloe-emodin. The detailed information about all these materials is shown in table S1.

The X-ray powder diffraction (XRPD) patterns of aloe-emodin were collected in air on a PANalytical Empyrean at room temperature using Cu KR radiation of wavelength 0.154060 nm, a tube voltage of 40 kV, and a tube current of 40 mA. Diffraction data were recorded at 2θ values between 3°and 45° at an interval of 0.05° and a continuous scanning speed of 5°·min^{-1} was employed. The XRPD pattern of aloe-emodin powders is illustrated in figure S1 and a characteristic peak at 8.16° is observed.

2.2. Measurement and analysis of aloe-emodin solubility

The solubility apparatus and procedure of aloe-emodin in seven different solvents are similar to those used in our previous work [24,25]. An excess amount of aloe-emodin was added to a 35 mL of the seven solvents with their temperatures ranging from (278.15 to 318.15) K at around 5 K increments under atmospheric pressure. A 0.45 μm pore syringe filter was used to take a sample of the liquid phase. Then, the concentration was measured by UV–vis spectrophotometer (TU-1810, Beijing Purkinje General Instrument Co. Ltd., Beijing, China).

During our experiments, two independent experiments were undertaken to check the aloe-emodin solubility. The maximum deviation from the average value was found to be ±5%, so it was proven that this experimental technique is reliable. The external calibration curve was obtained in ethanol and used for quantification of aloe-emodin in different solvents. The aloe-emodin in ethanol solution has obvious UV adsorption peaks at 255 nm, 287 nm and 383 nm, and the detection wavelength used in our experiments was chosen at 287 nm.

The mole fraction solubility of aloe-emodin in seven solvents was calculated using experimental values of solubility on the basis of the following equation:

$$x_1^{\exp} = \frac{m_1/M_1}{m_1/M_1 + m_2/M_2}, \tag{1}$$

where m_1 and m_2 are the masses of the solute and solvent, respectively; M_1 and M_2 represent the molecular weight of solute and solvent, respectively.

3. Results and discussion

3.1. Solubility of aloe-emodin

The solubility of aloe-emodin in water, methanol, ethanol, 1-propanol, 1-butanol, 2-butanol, and 1-pentanol at different temperatures are given in table 1. The temperature-dependent solubility of aloe-emodin in water is available in litreature [11,12]. The intrinsic solubility of aloe-emodin in water has been reported as 5.5×10^{-5} mole per liter at $T = 298$ K. Pan has reported the experimental solubility value of aloe-emodin as 2.29×10^{-6} mole per liter. In the present work, the solubility of aloe-emodin in water was observed as 2.16×10^{-5} mole per liter at $T = 298$ K. Our results were similarly reported by Fan *et al.* in their study. As can be seen from table 1, the solubility of aloe-emodin in all solvents increases with temperature and shows the positive dependency on temperature. The experimental mole solubility values of aloe-emodin in 1-pentanol, 1-butanol and 1-propanol were significantly higher than water and methanol. At constant temperature, each of the organic solvents shows greater solubility than water and the solubility of aloe-emodin in organic solvents is about 100 orders of magnitude higher than that in water. The $x_i^{\exp}$ values of aloe-emodin at $T = 298.15$ K were observed highest in 1-pentanol (13.77×10^{-5}) followed by 1-butanol (9.05×10^{-5}), 1-propanol (5.261×10^{-5}), 2-butanol (4.524×10^{-5}), ethanol (3.744×10^{-5}), methanol (0.5390×10^{-5}) and water (0.0807×10^{-5}).

The higher solubility values of aloe-emodin in solvents were probably due to lower solvent polarity which can be deduced by the decrease of the solvatochromic parameters except for 2-butanol. Wu and Zhang have found that the solubility of genistein increased with increasing polarity of the solvents to some extent [26]. The solvatochromic parameter E_T^N of 2-butanol is 0.506, however, the solubility values of aloe-emodin in 2-butanol is lower than those in 1-pentanol and 1-butanol. Maybe the 2-butanol has the branched structure and is not conducive to the aloe-emodin dissolved. The solvatochromic parameter E_T^N of 1-pentanol and water is 0.586 and 1.0, respectively, so the properties of solvent can remarkably influence the dissolution of aloe-emodin. All in all, straight chain mono alcohols can more easily dissolve aloe-emodin than in pure water or branched chain structure 2-butanol.

The relative deviation (RD), and the relative average deviation (RAD) are also listed in table 1. The RD is calculated according to the following formula:

$$\mathrm{RD} = \frac{\left|x_i^{\mathrm{cal}} - x_i^{\exp}\right|}{x_i^{\exp}}. \tag{2}$$

The RAD is calculated according to the following formula:

$$\mathrm{RAD} = \frac{\sum_{i=1}^{n} \frac{\left|x_i^{\mathrm{cal}} - x_i^{\exp}\right|}{x_i^{\exp}}}{n} \times 100\%, \tag{3}$$