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Determination and correlation of solubility of tylosin tartrate in alcohol mixtures

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ABSTRACT

Data on (solid + liquid) equilibrium of tylosin tartrate in {methanol + (ethanol, 1-propanol or 2-propanol)} solvents will provide essential support for industrial design and further theoretical studies. In this study, the solubility of tylosin tartrate in alcohol mixtures was measured over temperature range from (278.15 to 323.15) K under atmospheric pressure by a gravimetric method. From the experimental results, the solubility of tylosin tartrate in selected solvents noted above was found to increase with increasing temperature and mass fraction of methanol. The solubility data were correlated with the modified Apelblat equation, the λh equation and van't Hoff equation. The results showed that the three equations agreed well with the experimental values, and that the modified Apelblat equation was more accurate than the λh equation and van't Hoff equation. Further, the standard enthalpy, standard entropy and standard Gibbs free energy of solution of tylosin tartrate in mixed solvents were calculated according to solubility results, model parameters with modified Apelblat equation and van't Hoff equation.

1. Introduction

Tylosin tartrate (CAS Registry No: 74610-55-2) is a kind of the tylosin derivative and has the same antibiosis properties as tylosin. The chemical structure is shown in figure 1. Tylosin tartrate is a medium spectrum antibiotic not only used in veterinary medicine for the treatment of infections caused by most Gram-positive bacteria, mycoplasmas, some Gram-negative bacteria and Chlamydia [1–3], but also used as a feed additive to increase the rates of weight gain and improve the feed efficiency of companion animals, such as cattle, chicken, turkey, and swine [4–6]. But the residues of these antibiotics may stay in the edible tissue of animals and pose a threat to the health of humans when misused. Therefore, tylosin was banned as a growth promoter by the EU Commission in 1999 [7], disabled as drugs in fishery breeding by China's agricultural industry standards NY 5071-2002, and canceled from edible animal breeding by FDA in U.S in 2014 [8]. Maximum residue levels (MRLs) of these drugs in livestock products have been established in many countries [9–11].

For expanding the fields of usage and purification of tylosin tartrate, the data of (solid + liquid) equilibrium are required. Liquid alcohols play an important role and are widely used in industry and science research as reagents, solvents and fuels. The solubility of tylosin tartrate in alcohol solvents has not been published at present. Hence we measured solubility of tylosin tartrate in {methanol + (ethanol, 1-propanol or 2-propanol)} over the temperature range from (278.15 to 323.15) K under atmospheric pressure by a gravimetric method. The experimental values were correlated with the modified Apelblat equation, the λh equation and van't Hoff equation. The standard enthalpy, entropy and Gibbs free energy of solution of tylosin tartrate were calculated according to the modified Apelblat equation and van't Hoff equation.

2. Experimental

2.1. Materials

Tylosin tartrate ($C_{46}H_{77}NO_{17}{\cdot}C_4H_6O_6$, molar mass 1066.19) was obtained from Ningxia Tairui Pharmaceutical Co. Ltd., China and re-crystallized. Its mass faction purity was 0.99, which was determined by HPLC (type Agilent 1200, Agilent Technologies). It was dried in vacuum at $T = 23.15$ K for 24 h and stored in a desiccator. All the solvents (purchased from Tianjin Wind Ship Chemical Co. Ltd., China) were analytical reagent grade. Their mass fraction purities were better than 99.5% and were used without further treatment before use. The sources and mass fraction purity of the materials are given in table 1.

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2.2. Apparatus and procedure

In the experiment, the solubility of tylosin tartrate in alcohol mixed solvents was measured over temperature range from (278.15 to 323.15) K under atmospheric pressure by a gravimetric method. The experiment was carried out in a cylindrical double-jacketed glass vessel (120 mL) magnetically stirred. A constant temperature (±0.05 K) was controlled by circulating water from a water bath with a thermoelectric controller (type DC-2006, Shanghai Bilon Instruments Co., Ltd., China). For each measurement, the excess tylosin tartrate (±0.1 g) was added to a known mass of mixed solvents (±0.1 g). The supersaturated solution was stirred with a magnetic stirrer (type 85-1, Zhengzhou Yingyu Instrument factory, China) at a desired temperature for at least 12 h and then the solution was kept at least 2 h before sampling. The sample of approximately 2 mL was taken from clear saturated solution, filtered with membrane (0.45 μm) and placed in a weighed double dish (m_0), the sample in double dish was weighed (m_1) by an analytic balance with an uncertainty of ±0.1 mg (type FA2104N, Shanghai Jinghai Instruments Co., Ltd., China) and was transferred to a vacuum oven to dry at $T = 323.15$ K for 12 h [12–14]. All the solvent was completely evaporated; the double dish was reweighed (m_2) to determine the mass of solute. All the experiments were repeated three times at each temperature to obtain mean values. The mole fraction solubility x_i of tylosin tartrate in mixed solvents could be calculated by the following equation:

$$x_i = \frac{(m_2 - m_0)/M_1}{(m_2 - m_0)/M_1 + (m_1 - m_2) \times w/M_2 + (m_1 - m_2) \times (1 - w)/M_3}, \quad (1)$$

where M_1, M_2, M_3 represent the molar mass of tylosin tartrate, methanol and ethanol (or 1-propanol and 2-propanol), respectively, w is the mass fraction of methanol in mixtures. $(m_2 - m_0)$ and $(m_1 - m_2)$ represent the mass of the solute and mixed solvents in taken sample, respectively.

2.3. Experiment reliability

To identify the reliability of the measuring method, the solubility of potassium chloride in water was measured. Compared to literature data [15], results of solubility are shown in figure 2, where the experimental values for potassium chloride agree well with the literature and the deviation of solubility is less than 2%.

3. Results and discussion

3.1. Solubility data

Tylosin tartrate is a biological product and shows excellent stability at temperatures below 333.15 K [16,17], and that the boiling

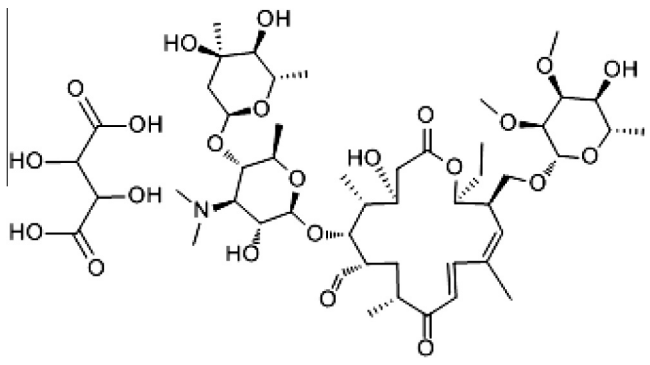

FIGURE 1. Molecular structure of tylosin tartrate.

TABLE 1
The sources and mass fraction purity of the materials.

Chemical name	Source	Mass fraction purity
Tylosin tartrate	Ningxia Tairui Pharmaceutical Co. Ltd	0.99
Methanol (AR)	Tianjin Wind Ship Chemical Co. Ltd.	0.995
Ethanol (AR)	Tianjin Wind Ship Chemical Co. Ltd.	0.997
1-Propanol (AR)	Tianjin Wind Ship Chemical Co. Ltd.	0.998
2-Propanol (AR)	Tianjin Wind Ship Chemical Co. Ltd.	0.997

AR means analytical reagent.

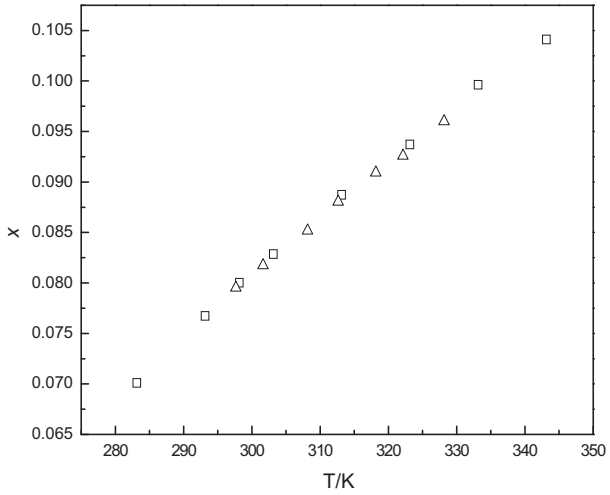

FIGURE 2. The solubility (x) of potassium chloride in water over the temperature range from (283.15 to 343.15) K: (△) this work; (□) literature [15].

points of selected solvents are lower. Therefore the solubility values of tylosin tartrate in alcohol mixtures within the temperature range from (278.15 to 323.15) K were determined by experiment. The results show in tables 2 and 3 and graphically in figures 3–5, respectively. The relative error (RD), the average absolute deviation (RAD) and the root-mean-square deviations (RMSD) are given in tables 2 and 3 and tables 4–6. The relative error (RD) is defined as follows:

$$\mathrm{RD} = \frac{|x_{cal} - x_i|}{x_i}. \quad (2)$$

The average absolute deviation (RAD) is defined as follows:

$$\mathrm{RAD} = \frac{\sum_{i=1}^{n} \frac{|x_{cal} - x_i|}{x_i}}{n} \times 100\% \quad (3)$$

The root-mean-square deviations (RMSD) is defined as follows:

$$\mathrm{RMSD} = \left[\sum_{i=1}^{n} \frac{(x_{cal} - x_i)^2}{n} \right]^{1/2}, \quad (4)$$

where n is the number of experimental points and $x_{i,cal}$ and x_i represent the calculated and the experimental solubility values, respectively.

From tables 2 and 3 and figures 3–5, it can be seen that solubility of tylosin tartrate increases with increasing mass fraction of methanol in mixed solvents at constant temperature and increases with increasing temperature at the same mass fraction. The solubility of tylosin tartrate in methanol is greater than in methanol mixture solvents, and in 2-propanol is the least. The reasons for this phenomenon may be the so-called "like dissolves like", polar molecules dissolve easily in polar solvent. The molecular structure of tylosin tartrate shows strong polarity