Fluid Phase Equilibria 360 (2013) 118–123

Contents lists available at ScienceDirect

Fluid Phase Equilibria

journal homepage: www.elsevier.com/locate/fluid

Measurement and correlation of the solubility of florfenicol in binary 1,2-propanediol + water mixtures from 293.15 K to 316.25 K

Jianyu Zhou, Hualin Fu*, Hang Cao, Chaocheng Lu, Chao Jin, Tao Zhou, Mengjiao Liu, Yanli Zhang

Department of Pharmacy, College of Veterinary Medicine, Sichuan Agricultural University, Yaan, Sichuan 625014, People's Republic of China

ARTICLE INFO

Article history:
Received 1 August 2013
Received in revised form 13 August 2013
Accepted 11 September 2013
Available online 19 September 2013

Keywords:
Florfenicol
Solubility
Static method
Solution thermodynamics

ABSTRACT

The solubility of florfenicol in mixed 1,2-propanediol + water solvents was measured by a static analytical method at the temperature ranging from 293.15 K to 316.25 K. The experimental solubility data was correlated by the modified Apelblat equation, the General Single model and the Hybrid model. The results show that: the mole solubility of florfenicol in binary 1,2-propanediol + water mixtures increased with increasing temperature and the mole fraction of 1,2-propanediol in the binary solvent system; the values of the solubility calculated by the three models show good agreement with the experimental value; the *OMPD* from the modified Apelblat equation, the General Single model and the Hybrid model are 2.48, 2.07 and 5.12, respectively. However, compared to the modified Apelblat equation and the Hybrid model, the General Single model can give more accuracy and reliability of the solubility data. In addition, the discussion of the enthalpy and the entropy for florfenicol in different cosolvents indicated that the dissolution process of florfenicol was endothermic and entropy-driven.

1. Introduction

The utilization of pharmaceuticals desires the unique solubility data involves liquid solvent selection, such as chemical reaction, pre-formulation, purification and liquid pharmaceutical product [1]. Thus, it is critically important to select the optimum solvents for a particular process. However, choosing solvents for pharmaceutical application has been based on experience. Therefore, a rapid and reliable method for measuring the solubility of drug is necessary for the design of pharmaceutical manufacture effectively.

Florfenicol (2,2-dichloro-N-[(1*R*,2*S*)-3-fluoro-1-hydroxy-1-(4-methylsulfonylphenyl)propan-2-yl] acetamide; $C_{12}H_{14}CL_2FNO_4S$; CAS No: 73231-34-2; Fig. 1) is a fluorinated synthetic analog of thiamphenicol and broad spectrum antibiotic, which belongs to a group of agents used in veterinary medicine named amphenicols [2,3]. In many countries, it can be used as a replacement for chloramphenicol (CAP) in the treatment of animal diseases and infections. The solubility of florfenicol in methanol, ethanol, acetone and so on has been reported in the literature [4]. However, some hazardous industrial solvents, such as methanol, acetone, etc., possess acute toxicity limiting their application in pharmaceutical preparations. It is well known that the solubility of florfenicol in neat water is too low, and some cosolvents containing water have been evaluated in order to increase the solubility. Moreover, 1,2-propanediol belonging to the nontoxic organic solvents [5] has been used almost exclusively in the production of water-insoluble drug [6]. Furthermore, it can be used as solvent and diluent in pharmaceutical preparations, which is a hydrogen-donor and hydrogen-acceptor compound, and thus, it is miscible with water in all proportions [7]. Thus, it is critically necessary to extend the database on experimental solubility for florfenicol to 1,2-propanediol + water binary mixtures at a certain temperature range.

In the present work, a static method was employed to measure the solubility of florfenicol in several different proportions of binary 1,2-propanediol + water mixtures at the temperature ranging from 293.15 K to 316.25 K. The experimental solubility data was correlated by the modified Apelblat equation, the General Single model and the Hybrid model. The thermodynamic properties of the dissolution process for this system, including the enthalpy and the entropy obtained by van't Hoff equation, was discussed as well.

2. Experimental

2.1. Materials

The materials table is depicted in Table 1.

* Corresponding author. Tel.: +86 0835 2885614.
E-mail address: zhoujianyu2014@gmail.com (H. Fu).

0378-3812/$ – see front matter.
http://dx.doi.org/10.1016/j.fluid.2013.09.020

Table 1
Characteristics of chemicals used in this study.

Chemical name	Source	Initial mass fraction purity	Purification method	Final mass fraction purity	Analysis method
Methanol	Tianjin Kermel Chemical Reagent Co., Ltd.	≥99.8%	None	–	–
1,2-Propanediol				–	–
Florfenicol	Hubei Zhongmu Anda Pharmaceutical Co., Ltd.	≥98.5%	Purified by recrystallization from acetone three times, and dried at 343.15 K for 24 h	≥99.6%	UV[a]
Water	Double-distilled water prepared by the laboratory	–	None	–	–

[a] Ultraviolet spectrophotometry.

2.2. Apparatus and procedure

The equilibrium solubility data was measured by a static method, and this procedure used in this research was similar to the literature [8,9]. All 1,2-propanediol + water solvent mixtures were prepared, using an ESJ200-4B analytical balance with sensitivity of ±0.0001 g, in quantities of 45.00 g. Taken the viscosity of 1,2-propanediol into consideration, the mass fractions of 1,2-propanediol, w, were prepared varied by 0.15 from 0.05 to 0.65 in addition to a group without 1,2-propanediol. An excess of florfenicol was added into a 150 ml volumetric Erlenmeyer flask with a rubber plug. The Erlenmeyer was placed in a thermostatic mechanical shaker (HZS-H water bath oscillator, china) for 48 h to reach solid–liquid equilibrium. The temperature of the inner Erlenmeyer flask was corrected by a mercury thermometer (uncertainty of ±0.05 K).

A certain volumetric mixtures were drawn by a preheated pipette after the equilibrium was reached. The samples were filtered through microporous membrane (0.22 μm) of the organic phase before analysis. A certain volume (5 ml) of the mixtures was removed by a precise preheated pipette (uncertainty of 0.05 ml) which was calibrated to weigh the mass and calculate the density. Then 2 ml samples were transferred to volumetric flask in addition to the liquid of the precise pipette washed by methanol 3 times to a suitable dilution with methanol. According to the standard curve constructed by plotting concentration versus absorbance (Fig. 2), the concentrations of florfenicol were analyzed by UV spectrophotometer (WFZ UV-2000, Unico, china) at 266 nm wavelength. The solubility data was repeated three times and the mean values were used to calculate the mole solubility.

The mass of the solute in 1 ml mixtures was expressed by Eq. (1). The initial mass fraction of 1,2-propanediol in mixtures, w, can be defined as Eq. (2), and the mole faction composition of 1,2-propranediol, x_0, can be obtained by Eq. (3). The mole fraction solubility of solute in 1 ml mixtures, x_1, could be obtained by Eq. (4).

$$m_1 = \frac{cn}{v} \tag{1}$$

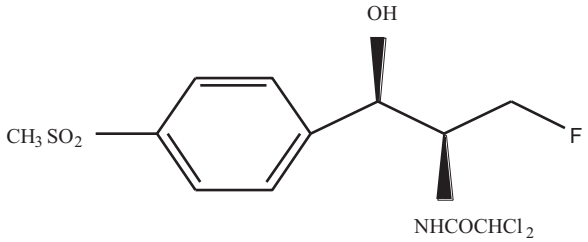

Fig. 1. Chemical structure formula of florfenicol.

where c respects the concentration of the sample analyzed based on the standard curve, m_1 is the mass of solute in 1 ml mixtures, and v, n refer to the volume and dilution ratio of the samples analyzed, respectively.

$$w = \frac{m_p}{m_p + m_w} \tag{2}$$

$$x_0 = \frac{(m - m_1)w/M_p}{(m - m_1)w/M_p + (m - m_1)(1 - w)/M_w} \tag{3}$$

$$x_1 = \frac{m_1/M_1}{m_1/M_1 + (m - m_1)w/M_p + (m - m_1)(1 - w)/M_w} \tag{4}$$

where m represents the mass of 1 ml mixtures. m_p and m_w are the initial mass of 1,2-propanediol and water introduced. M_0, M_w, and M_1 represent the molecular mass of 1,2-propanediol, water and solute, respectively. The uncertainty of the solubility values is estimated to be ±0.0001.

The *RD* between the calculated and the experimental values are calculated according to Eq. (5).

$$RD = \frac{x_1 - x_1^{cal}}{x_1} \tag{5}$$

The mean percentage deviation (*MPD*) defined in Eq. (6) was used to evaluate the agreement between the experimental data and the model predictions.

$$MPD = \frac{100}{N} \sum \frac{\left|x_1 - x_1^{cal}\right|}{x_1} \tag{6}$$

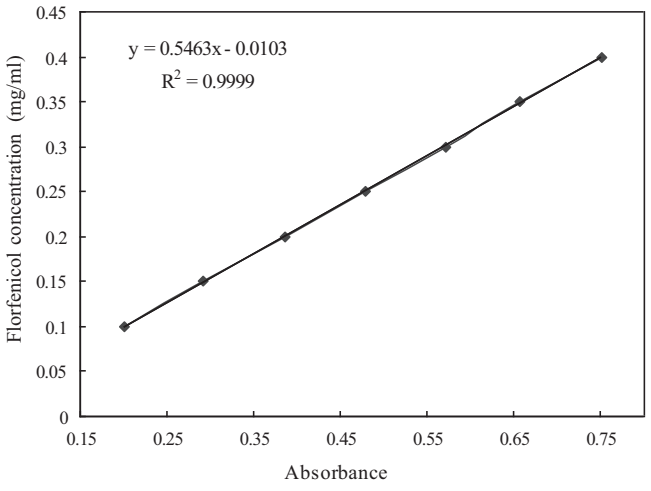

Fig. 2. Standard curve for the dependence of florfenicol concentration on UV absorbance.