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Volumetric and transport properties of betaine hydrochloride drug in aqueous uracil solutions at $T = (298.15–318.15)$ K

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ABSTRACT

Apparent molar volumes and viscosity *B*-coefficients for betaine hydrochloride in aqueous uracil solutions were determined from solution densities and viscosities measured at $T = (298.15–318.15)$ K and at pressure $p = 101$ kPa as a function of betaine hydrochloride concentrations. The standard partial molar volumes (ϕ_V^0) and slopes (S_V^*) obtained from Masson equation were interpreted in terms of solute–solvent and solute–solute interactions, respectively. Solution viscosities were analyzed using Jones–Dole equation and the viscosity *A* and *B* coefficients discussed in terms of solute–solute and solute–solvent interactions, respectively. The standard volume of transfer $(\Delta_t\phi_V^0)$ and viscosity *B*-coefficients of transfer $(\Delta_t B)$ of betaine hydrochloride from water to aqueous uracil solutions were derived to understand various interactions in the ternary solutions. The activation parameters of viscous flow for the studied solutions were discussed in terms of transition state theory. The structure making or breaking ability of betaine hydrochloride was discussed in terms of the sign of $(d\phi_E^0/dT)_p$.

1. Introduction

Volumetric and viscometric properties provide valuable information regarding the behaviour of various solutes such as proteins, peptides, drugs, nucleotides, carbohydrates in aqueous or non-aqueous media [1–8]. Understanding the action of drugs and their interaction with different biologically important compounds is a subject of research interest. These interactions provide idea about the activity of drug in biological systems. As the drug action is difficult to understand, different thermodynamic and rheological properties such as density and viscosity are used to interpret the drug-macromolecule interactions.

Betaine hydrochloride drug (B.HCl) is used for supplementing low stomach acid which is a key component of our immune system and it is also used as a digestive pill for the human body. In some cases it may also used for the treatment of food allergies, diarrhoea, thyroid disorder and low level of potassium. Uracil is one of the four nucleobases in the nucleic acid of RNA. It helps the body to synthesize many enzymes necessary for cell functioning. It is also used as a allosteric regulator in the body. It can be used for drug delivery. It is therefore interesting to observe the interaction between B.HCl and uracil in aqueous media.

Many studies on the thermodynamic and rheological properties of drugs have been carried out by a number of researchers [8–13]. Gardas et al., studied the acoustic and volumetric properties of betaine hydrochloride drug in aqueous glucose and sucrose solutions [14]. To the best of our knowledge from the literature survey, the values of density and viscosity of B.HCl drug in aqueous uracil solutions have not been reported at the concentrations and temperatures investigated in this article.

Hence the purpose of the present work is to study the various interactions interplaying in the aqueous solutions of B.HCl drug and uracil in terms of apparent molar volumes, standard partial molar volumes and viscosity *B*-coefficients, *etc.*, at $T = (298.15–318.15)$ K under atmospheric pressure.

2. Experimental

2.1. Materials

Betaine hydrochloride, $[(CH_3)_3NCH_2COOH]^+\ Cl^-$ (CAS: 590-46-5; Sigma Aldrich, mass fraction purity >0.990) and premium grade Uracil, $C_4H_4N_2O_2$ (CAS: 66-22-8; Sigma Aldrich, mass fraction purity >0.990). Betaine hydrochloride and uracil were used without further purification but they were dried in *vacuo* over anhydrous $CaCl_2$ for several hours before use. Provenance and purity of the chemicals has been given in Table 1. Deionized doubly distilled degassed water with a specific conductance $<10^{-6}$ S cm^{-1} was used

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Table 1
Provenance and purity of the chemicals used.

Chemical	Source	Purification method	Mass fraction purity	CAS No
Betaine hydrochloride	Sigma–Aldrich	None	0.990	590-46-5
Uracil	Sigma–Aldrich	None	0.990	66-22-8

for the preparation of aqueous solutions of uracil. Various mixed solvents were prepared by mass and necessary adjustments were done to achieve exact molality ($m_{Uracil} = 0.005$, 0.010, 0.015 and 0.020) of uracil in the mixed solvents at 298.15 K. The physical properties of these mixed solvents are given in Table S1. A comparison of density data for the aqueous uracil solutions and aqueous betaine hydrochloride solutions with available literature data was given as Supplementary Fig. S3 [14–17].

Stock solutions of betaine hydrochloride in different solvent mixtures were prepared by mass and all the working solutions were prepared afresh before use by mass dilution. The mass measurements were made on a digital electronic analytical balance (Mettler, AG 285, Switzerland) with an uncertainty of $\pm 1 \times 10^{-4}$ g. The conversion of molalities into molarities was accomplished by using experimental densities whenever needed [18]. Standard relative uncertainty in molality of betaine hydrochloride solutions i.e., $u_r(m)$ was evaluated to 0.01. The molecular structure of betaine hydrochloride and uracil are shown in Fig. 1.

2.2. Apparatus and procedure

The densities were measured with a vibrating-tube density meter (Anton Paar, DMA 4500M). The densitometer was calibrated at the experimental temperatures with doubly distilled, degassed water and dry air at atmospheric pressure. The temperature was automatically kept constant with an accuracy of $\pm 1 \times 10^{-2}$ K using the built in Peltier technique. The stated repeatability and accuracy of the densities were $\pm 1 \times 10^{-5}$ g cm^{-3} and $\pm 5 \times 10^{-5}$ g cm^{-3} respectively. However, standard uncertainty of the density measurements for most of the solutions was found to be within the range ±0.1 kg m^{-3}. The viscosity was measured by means of a suspended Canon-type Ubbelohde viscometer thoroughly cleaned, dried and calibrated at the experimental temperatures with triply distilled, degassed water and purified methanol [19,20]. It was filled with an experimental liquid and placed vertically in a glass sided thermostatic bath (Julabo, Germany) maintained constant to ±0.01 K. After attainment of thermal equilibrium, the efflux times of flow of the liquid samples were recorded with a digital stopwatch correct to ±0.01 s. sufficient precautions were adopted to minimize evaporation loses during the viscosity measurements and an average of triplicate measurements was taken into account. Standard uncertainty in viscosity measurements was evaluated to be 0.01 mPa s.

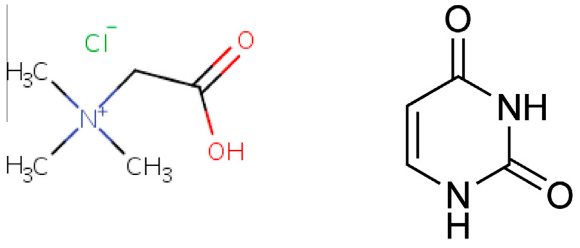

Fig. 1. Molecular structure of betaine hydrochloride. Molecular structure of uracil.

3. Results and discussion

The experimental molalities (m), densities (ρ), viscosities (η), and apparent molar volumes (ϕ_V) of betaine hydrochloride solutions in various aqueous uracil solutions (used as solvents) at the experimental temperatures are reported in Table S2.

3.1. Standard partial molar volumes

The apparent molar volume (ϕ_V) of a solute is defined as the difference between the volume of the solution and the volume of the pure solvent per mole of solute [21–23]. The apparent molar volumes (ϕ_V) were obtained from the following relation:

$$\phi_V = \frac{M}{\rho} - \frac{1000(\rho - \rho_1)}{m\rho\rho_1} \tag{1}$$

where M is the molar mass of betaine hydrochloride, m is the molality of the solution, ρ_1 and ρ are the densities of the solvent and solution, respectively. Uncertainties in ϕ_V values were within the range $\pm(0.12 - 0.67) \times 10^{-6}$ m^3 mol^{-1}. Table S2 shows that apparent molar volumes (ϕ_V) increase with increasing temperature and uracil-content in the ternary mixtures. Such trends indicate that the interactions between solute and solvent as well as those between solute–solute or solute–cosolute change with temperature and solvent compositions. However, limiting apparent molar volumes at infinite dilution or standard partial molar volumes (ϕ_V^0) of the solute can provide further information regarding solute–solute or solute–solvent interactions. ϕ_V values were observed to correlate linearly with the square root of solution molalities ($\sqrt{m}$) at all experimental temperatures, hence standard partial molar volumes (ϕ_V^0) were obtained from Masson equation [24]:

$$\phi_V = \phi_V^0 + S_V^* \sqrt{m} \tag{2}$$

Actually the ϕ_V^0 values were determined by fitting the dilute data ($m < 0.1$) to Eq. (2) using a weighted least squares linear regression and the correlation coefficients (R^2) were within the range 0.9795–0.9990. The weighting factor was set equal to the inverse of the variances of the ϕ_V values for each data point. The intercept ϕ_V^0, *i.e.*, the standard partial molar volume provides a measure of ion–solvent interactions and the slope S_V^* provides information regarding ion–ion interactions. The values of ϕ_V^0 and S_V^* along with standard deviations (σ) for betaine hydrochloride in different aqueous uracil solutions at the experimental temperatures are reported in Table 2. The ϕ_V^0 value is a measure of ion–solvent or solute–solvent interactions and the Table 2 shows that ϕ_V^0 values are positive and increase when both the experimental temperature and uracil content in the solvents increase. This trend in ϕ_V^0 values indicates the presence of strong solute–solvent interactions and such interactions further strengthen at elevated temperatures and with higher concentrations of uracil in the ternary solutions and such a trend in ϕ_V^0 values is at par the trends in ϕ_V values (as listed in Table S2) for the studied solutions. Dependence of ϕ_V^0 values on the solvent composition is depicted in Fig. 2.