Journal of Molecular Liquids 177 (2013) 49–53

Contents lists available at SciVerse ScienceDirect

Journal of Molecular Liquids

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

Viscometric measurements of L-serine with antibacterial drugs ampicillin and amoxicillin at different temperatures: (305.15 to 315.15) K

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ARTICLE INFO

Article history:
Received 31 July 2012
Accepted 23 September 2012
Available online 4 October 2012

Keywords:
L-Serine
Ampicillin
Amoxicillin
Viscosity
Viscosity *B*-coefficient

ABSTRACT

The viscosities, η of L-serine with drug ampicillin (AMP) and amoxicillin (AMX) have been measured as a function temperature at $T = (305.15, 310.15$ and $315.15)$ K. The viscosity data have been utilized to determine viscosity *B*-coefficients employing the Jones–Dole equation. The trends of variation in viscosity values of amino acid with an increase in molal concentration of AMP and AMX solutions and also with an increase in temperature have been ascribed to the solute–solvent interactions operative in the solutions. The activation parameters of viscous flow have been obtained to throw light on the mechanism of viscous flow. These parameters have been discussed in the light of ion–ion and ion–solvent interactions.

1. Introduction

Drug macromolecular interactions involved in drug transport, protein binding and anesthesia are important phenomena in physiological media [1]. The mechanisms of these molecular processes are not yet clearly understood. Attempts are being made to understand these interactions through the properties like partial molar volume, partial molar compressibility and viscosity studies [2,3]. As regards biomolecules, studies on amino acids have been made by Millero [4] and only these measurements have been adopted for a few drug molecules [5]. Despite years of investigations, many important drug actions [6] and their mechanisms are not fully understood. Among drugs broad spectrum penicillins like ampicillin and amoxicillin constitutes major budget of hospitals. Several experimental investigations have been carried out to understand the action of drugs in aqueous solution [7,8] as they exert their activity by interaction with biological membrane. Physicochemical and thermodynamic investigations also attract the inquisitive minds of researchers owing to the important role that drugs play to understand the nature and the extent of the patterns of molecular aggregation that exist in binary or ternary liquid mixtures [9,10] and their sensitivities to variations in composition and the molecular structure of the pure components [11]. Various concepts regarding molecular processes in solutions, electrostriction [12], hydrophobic hydration [13], micellization [14], and cosphere overlap during solute–solute interactions [15] to a large extent have been derived and interpreted from the partial molar volume data of many compounds. In biophysical chemistry, drug-macromolecular interaction is an important phenomenon involving a complex mechanism [16]. Viscosity studies of solution provide valuable information regarding the solute–solvent interactions. Structure making and breaking effects of an electrolyte on solvent can be determined by various parameters resolved from viscosity studies. A number of researchers have determined viscosity *B*-coefficients of amino acids and peptides in aqueous media [17–22] and in aqueous drug solutions [23]. Recent literature on the physical and thermodynamics studies of drugs and other materials of biological importance shows increasing interest by number of workers in this area of study [24–28]. As per our knowledge no data on thermodynamic studies of ampicillin and amoxicillin with amino acids have been reported so far. Moreover, no systematic studies are available on transport as well as thermodynamic properties of amino acids having polar side group (chain) i.e. serine which is a non essential amino acid and neutral in nature having one OH group which gives an additional propensity for interactions in situ conditions i.e. the temperature chosen for the present study is our body temperature 37 °C and 5 °C higher and lower of our body temperature in the presence of drug solutions. As part of the long term objective to investigate the thermodynamics studies [29,30] and various aspects of drug–macromolecular interactions [31], we report the results of determination of viscosity of two drugs i.e. ampicillin and amoxicillin which is amphoteric in nature with simple amino acid like serine.

2. Experimental

Ampicillin (AMP) and amoxicillin (AMX) with mass fraction purity >0.99 was obtained from M P Biomedicals, USA and was used as such without further purification. L-Serine of mass fraction purity >0.995

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http://dx.doi.org/10.1016/j.molliq.2012.09.016

was obtained from Merck, Germany and was used after recrystallization twice from ethanol–water mixtures. The amino acid was dried at $T=$ 373 K for 12 *h* in an infrared drier and then in vacuum over P_2O_5 at room temperature for at least 48 *h*. All the solutions were made afresh in triply distilled, degassed water having specific conductance less than 10^{-6} ohm cm^{-1} on Sartorius 210 S balance having precision of 0.0001 g. Uncertainty in the solution concentration was estimated at $\pm 2\times10^{-5}$ mol kg^{-1} in calculations. The details of the chemicals used in the present work are also given in Table 1.

Viscosities of solutions were determined using an Anton Paar Automated MicroViscometer (AMVn). The temperature was controlled to ± 0.01 K by a built in Peltier thermostat. The measurement method of this instrument was the falling ball principle. The sample was introduced into a calibrated glass capillary with a steel ball. The ball falling time was used to determine the viscosities. The calibration of capillary was performed by the manufacturer using viscosity standard fluids. The estimated experimental uncertainty in viscosity was estimated to be less than ± 0.0015 mPa S.

3. Results and discussion

Experimental data of viscosities, η, for L-serine in (0.0009, 0.0018, 0.0028 and 0.0038) mol kg^{-1} aqueous solutions of ampicillin and amoxicillin were measured at $T=$ (305.15, 310.15, and 315.15) K and reported in Table 2. Fig. 1 shows the experimental viscosities for L-serine in 0.0018 mol·kg^{-1}aqueous AMP and AMX solutions at different temperatures. The viscosity values have been found to be increasing with an increase in concentration of amino acid as well as increase in the concentration of drug solutions. The viscosity values of L-serine increases with increase in the concentration of AMP and AMX. This may be attributed to an increase in the solute–solvent (zwitterions–ions) interactions with successive increase in the number of amino acid molecules / zwitterions in solutions, which may in turn cause more frictional resistance to the flow of solutions. The viscosity values decreases with an increase in temperature. The increase in temperature may have caused the increase in the kinetic energy of molecules and ions present in the solution, which in turn decrease the solute–solvent interaction. Thus, the forces of attraction, which the moving solute and solvent molecules and ions have to overcome, intrinsically decrease with an increase in the random motion of molecules and ions as temperature increases which causes rapid movement of molecules and ions into the empty sites. Such a decrease in interactions seems to be responsible for the decrease in viscosity with an increase in temperature.

The variation of relative viscosity η_r for amino acid in aqueous AMP and AMX solutions and can be represented by Jones–Dole equation [32]

$$(\eta_r-1)/C^{1/2} = A + BC^{1/2} \quad (1)$$

where $\eta_r=\eta/\eta_0$ and η, η_0 are the viscosities of the solution and solvent (AMP + water) respectively, *A* and *B* are the constants characteristics of ion–ion and ion–solvent interactions, respectively. The *A* and *B* coefficients have been obtained by least square method by fitting the experimental data in Jones–Dole equation. The *A*-coefficient is independent of concentration and *B*-coefficient is related to the effect of amino acids on the structure of solvents. These values of *A*-coefficient and *B*-coefficient are reported in Table 3. The values of *B*-coefficients are also shown in Fig. 2. It is observed from Table 3 that the values of

Table 1
Specification of chemical samples.

Chemical name	Provenance	Mass fraction purity
L-Serine	Merck, Germany	>0.995
Ampicillin	M P Biomedicals, USA	>0.99
Amoxicillin	M P Biomedicals, USA	>0.99

Table 2
Viscosities (η) of serine in aqueous solutions of AMP at different temperatures.

$\frac{m}{(\text{mol kg}^{-1})}$	$\frac{\eta}{(\text{mPa s})}$		
	$T=305.15$ K	$T=310.15$ K	$T=315.15$ K
Serine + 0.0009 mol kg^{-1} ampicillin			
0.00000	0.7618	0.6924	0.6342
0.00244	0.7662	0.6979	0.6377
0.00327	0.7669	0.6988	0.6403
0.00452	0.7706	0.7022	0.6433
0.00607	0.7719	0.7046	0.6455
0.00834	0.7735	0.7076	0.6479
0.00979	0.7755	0.7098	0.6501
0.01274	0.7781	0.7112	0.6555
0.01484	0.7795	0.7139	0.6582
0.01680	0.7802	0.7169	0.6607
Serine + 0.0018 mol kg^{-1} ampicillin			
0.00000	0.7637	0.6948	0.6356
0.00268	0.7671	0.7007	0.6398
0.00415	0.7685	0.7039	0.6423
0.00568	0.7709	0.7053	0.6463
0.00735	0.7727	0.7095	0.6479
0.00849	0.7748	0.7102	0.6505
0.01002	0.7762	0.7123	0.6534
0.01265	0.7789	0.7136	0.6592
0.01571	0.7803	0.7157	0.6621
0.01747	0.7812	0.7191	0.6646
Serine + 0.0028 mol kg^{-1} ampicillin			
0.00000	0.7649	0.6964	0.6381
0.00242	0.7682	0.7012	0.6423
0.00434	0.7696	0.7055	0.6442
0.00648	0.7721	0.7076	0.6471
0.00855	0.7752	0.7095	0.6498
0.01091	0.7774	0.7112	0.6539
0.01298	0.7785	0.7149	0.6605
0.01488	0.7814	0.7163	0.6639
0.01790	0.7825	0.7203	0.6658
Serine + 0.0038 mol kg^{-1} ampicillin			
0.00000	0.7656	0.6976	0.6398
0.00232	0.7691	0.7032	0.6442
0.00422	0.7709	0.7062	0.6456
0.00619	0.7733	0.7084	0.6479
0.00883	0.7761	0.7104	0.6519
0.01017	0.7782	0.7122	0.6548
0.01263	0.7796	0.7143	0.6574
0.01558	0.7824	0.7178	0.6625
0.017159	0.7858	0.7198	0.6661
Serine + 0.0009 mol kg^{-1} amoxicillin			
0.00000	0.7642	0.6984	0.6386
0.00277	0.7681	0.7042	0.6441
0.00565	0.7696	0.7095	0.6501
0.00735	0.7736	0.7119	0.6525
0.00924	0.7768	0.7132	0.6551
0.01244	0.7804	0.7145	0.6591
0.01526	0.7846	0.7167	0.6648
0.01733	0.7897	0.7195	0.6678
0.01946	0.7929	0.7214	0.6688
Serine + 0.0018 mol kg^{-1} amoxicillin			
0.00000	0.7659	0.6991	0.6392
0.00281	0.7695	0.7051	0.6448
0.00487	0.7703	0.7107	0.6512
0.00673	0.7746	0.7143	0.6533
0.00885	0.7775	0.7157	0.6568
0.01075	0.7783	0.7181	0.6608
0.01429	0.7852	0.7197	0.6666
0.01722	0.7905	0.7206	0.6708
0.01899	0.7939	0.7221	0.6723
Serine + 0.0028 mol kg^{-1} amoxicillin			
0.00000	0.7668	0.7014	0.6401
0.00271	0.7701	0.7062	0.6459
0.00434	0.7718	0.7113	0.6522
0.00606	0.7739	0.7151	0.6549
0.00858	0.7789	0.7179	0.6576