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Transport behavior of L-alanine, L-valine and L-leucine in ampicillin solutions over temperature range (305.15 to 315.15) K

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ABSTRACT

The viscosities, η of L-alanine, L-valine and L-leucine with drug ampicillin (AMP) have been measured as a function of 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 acids with an increase in molal concentration of AMP 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

To understand the action of drugs in aqueous solution has always been a subject of research as they exert their activity by interaction with biological membrane. In biophysical chemistry, drug-macromolecular interaction is an important phenomenon involving a complex mechanism [1]. The studies on the thermodynamic and transport properties of drugs in aqueous as well as with biomolecules (proteins, enzymes and hormones) provide useful information in pharmaceutical and medicinal chemistry [2,3]. The interactions of water with the various functional groups of proteins play important factor in determining the conformational stability of proteins [4].

In recent years, there has been considerable interest in the determination of various thermodynamic, transport, surface properties, kinetic and UV studies of proteins and model compounds like amino acids and dipeptides which mimic some aspect of proteins and provide insight into different phenomena of proteins [5–8]. Ampicillin is a part of aminopenicillin family. The drug interactions occurring outside the body may be categorized as physical or chemical and may occur during formulation, storage as well as while mixing the ingredients [9]. Sometimes *in vitro* interaction occurs without any observable change like precipitation or color changes and therefore can be determined quantitatively by determining their thermodynamic properties in the solution [10]. The pharmacodynamics, pharmacokinetics, safety and efficacies of ampicillin have been widely evaluated [11].

A number of workers have studied the viscometric properties of amino acids and peptides in aqueous salt solutions [12–16]. Structure making and breaking effects of an electrolyte on solvent can be determined by various parameters resolved from viscosity studies. The Jones–Dole viscosity B-coefficients depend on both the size of solute and solute–solvent interactions. A number of researchers have determined viscosity B-coefficients of amino acids and peptides in aqueous media [17–23], in aqueous polyethylene glycol and polyvinylpyrrolidone which is used as a hydrophilic carrier and is a commonly used method to improve drug solubility [24,25] and viscosity B-coefficients have also been found for aqueous drug solutions [26–29] but very few has been directed towards the interactions of amino acids with antibacterial drugs like ampicillin. Though, some work have been carried out on enthalpy of solution of ampicillin, amoxicillin and their binary mixtures and microcalorimetric evaluation of *in vitro* compatibility of amoxicillin/clavulanic acid and ampicillin/sulbactam with ciprofloxacin [30]. As per our knowledge, no data on thermodynamic studies of ampicillin with amino acids have been reported so far.

In continuation to our work on thermodynamic studies [31–33] of amino acids, our focus in this present paper is to study interactions of antibacterial drug ampicillin that is amphoteric in nature with simple amino acids like alanine, valine and leucine *in situ* conditions with the

Table 1
Specification of chemical samples.

Chemical name	Provenance	Mass fraction purity
Ampicillin	M P Biomedicals, USA	>0.99
L-Alanine	Merck, Germany	>0.995
L-Valine	Merck, Germany	>0.995
L-Leucine	Merck, Germany	>0.995

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help of viscometric data. Temperature chosen for the present study is our body temperature 37 °C and 5 °C higher and lower of our body temperature. In the present study, we report the viscosities of L-alanine, L-valine and L-leucine in (0.0006, 0.001, 0.002, and 0.004) mol kg^{-1} solutions of ampicillin (AMP) at T = (305.15, 310.15 and 315.15) K.

The drug–AA molecular interaction and their temperature dependence play an important role in the understanding of drug action. Such results can be helpful in predicting the absorption of drugs and transport of drugs across the biological membranes. Therefore, it may be interesting to investigate variation of their properties with temperature for understanding the mechanism of drug action.

Table 2
Viscosities (η) of alanine, valine and leucine in aqueous solutions of AMP at different temperatures.

η/(mPa s)			
m/(mol kg^{-1})	T = 305.15 K	T = 310.15 K	T = 315.15 K
Alanine + 0.0006 mol kg^{-1} ampicillin			
0.00000	0.7569	0.6941	0.6361
0.00231	0.7585	0.6956	0.6384
0.00478	0.7616	0.6972	0.6395
0.00625	0.7676	0.7015	0.6418
0.00813	0.7713	0.7056	0.6426
0.01129	0.7821	0.7129	0.6436
0.01561	0.7919	0.7149	0.6488
Alanine + 0.001 mol kg^{-1} ampicillin			
0.00000	0.7630	0.6965	0.6376
0.00207	0.7677	0.6991	0.6392
0.00468	0.7687	0.7013	0.6401
0.00647	0.7769	0.7067	0.6433
0.00883	0.7851	0.7182	0.6449
0.01041	0.7906	0.7211	0.6515
0.01253	0.7958	0.7246	0.6639
Alanine + 0.002 mol kg^{-1} ampicillin			
0.00000	0.7702	0.6989	0.6407
0.00362	0.7723	0.7039	0.6498
0.00433	0.7735	0.7056	0.6507
0.00620	0.7808	0.7085	0.6523
0.00812	0.7866	0.7099	0.6535
0.01022	0.7991	0.7147	0.6616
0.01264	0.8095	0.7266	0.6636
Alanine + 0.004 mol kg^{-1} ampicillin			
0.00000	0.7730	0.7041	0.6421
0.00219	0.7746	0.7056	0.6519
0.00266	0.7753	0.7069	0.6538
0.00400	0.7821	0.7107	0.6546
0.00618	0.7972	0.7218	0.6576
0.00822	0.8025	0.7327	0.6661
0.01006	0.8157	0.7397	0.6681
Valine + 0.0006 mol kg^{-1} ampicillin			
0.00000	0.7569	0.6941	0.6361
0.00253	0.7592	0.6965	0.6387
0.00334	0.7628	0.6978	0.6412
0.00629	0.7642	0.7022	0.6437
0.00789	0.7679	0.7063	0.6444
0.00891	0.7707	0.7097	0.6504
0.01087	0.7726	0.7127	0.6521
0.01304	0.7784	0.7145	0.6534
0.01462	0.7806	0.7176	0.6547
Valine + 0.001 mol kg^{-1} ampicillin			
0.00000	0.7630	0.6965	0.6376
0.00229	0.7680	0.7002	0.6417
0.00428	0.7700	0.7053	0.6432
0.00628	0.7788	0.7092	0.6452
0.00802	0.7864	0.7193	0.6532
0.01085	0.7932	0.7234	0.6593
0.01291	0.7991	0.7301	0.6682
Valine + 0.002 mol kg^{-1} ampicillin			
0.00000	0.7702	0.6989	0.6407
0.00195	0.7799	0.7011	0.6478
0.00352	0.7866	0.7113	0.6508
0.00425	0.7871	0.7126	0.6564
0.00575	0.7939	0.7212	0.6625
0.00679	0.8013	0.7295	0.6701
0.00778	0.8027	0.7314	0.6726
0.01066	0.8092	0.7396	0.6803
0.01182	0.8165	0.7473	0.6896

Table 2 (*continued*)

η/(mPa s)			
m/(mol kg^{-1})	T = 305.15 K	T = 310.15 K	T = 315.15 K
Valine + 0.004 mol kg^{-1} ampicillin			
0.00000	0.7730	0.7041	0.6421
0.00296	0.7809	0.7165	0.6523
0.00435	0.7823	0.7182	0.6603
0.00623	0.7976	0.7225	0.6628
0.00801	0.8038	0.7331	0.6712
0.01024	0.8121	0.7402	0.6812
0.01273	0.8219	0.7525	0.6927
Leucine + 0.0006 mol kg^{-1} ampicillin			
0.00000	0.7569	0.6941	0.6361
0.00263	0.7638	0.6979	0.6412
0.00414	0.7653	0.6994	0.6452
0.00617	0.7688	0.7037	0.6468
0.00828	0.7714	0.7149	0.6471
0.01043	0.7775	0.7168	0.6552
0.01243	0.7792	0.7278	0.6563
Leucine + 0.001 mol kg^{-1} ampicillin			
0.00000	0.7630	0.6965	0.6376
0.00203	0.7693	0.7077	0.6467
0.00415	0.7719	0.7098	0.6474
0.00684	0.7796	0.7149	0.6489
0.00820	0.7871	0.7198	0.6577
0.01029	0.7946	0.7316	0.6614
0.01328	0.8012	0.7402	0.6705
Leucine + 0.002 mol kg^{-1} ampicillin			
0.00000	0.7702	0.6989	0.6407
0.00223	0.7823	0.7164	0.6553
0.00489	0.7860	0.7196	0.6687
0.00626	0.7986	0.7293	0.6689
0.00845	0.7998	0.7368	0.6793
0.01019	0.8114	0.7455	0.6899
0.01217	0.8186	0.7514	0.6942
Leucine + 0.004 mol kg^{-1} ampicillin			
0.00000	0.7730	0.7041	0.6421
0.00217	0.7835	0.7182	0.6617
0.00448	0.7863	0.7223	0.6721
0.00625	0.8011	0.7345	0.6832
0.00793	0.8129	0.7431	0.6925
0.01066	0.8221	0.7653	0.7123
0.01396	0.8378	0.7703	0.7217

2. Experimental

Ampicillin (AMP) with mass fraction purity > 99% was obtained from M P Biomedicals, USA. Alanine, valine and leucine of mass fraction purity > 99.5% were obtained from Merck, Germany. All the amino acids used were of L-configuration. All the chemicals were used as such without further purification. However, before use amino acids were dried under vacuum. Thereafter, they were stored over P_2O_5 in desiccators for minimum of 48 h before use. Double distilled water (specific conductance $<10^{-6}$ S cm^{-1}) which has been freshly degassed was used for the preparation of the aqueous solutions. 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