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Der Pharma Chemica, 2015, 7(12):219-226 (http://derpharmachemica.com/archive.html)



ISSN 0975-413X CODEN (USA): PCHHAX

Molecular interaction study of aqueous solution of an aminoglycoside antibiotic Neomycin at 298.15 to 308.15 K

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ABSTRACT

Ultrasonic velocity, density, and viscosity of aqueous solutions of aminoglycoside antibiotic- Neomycin sulphate at three different temperatures 298.15, 303.15 and 308.15K, for various concentrations (0.0010 - 0.1003) mol.kg⁻¹ have been measured. From the experimental data, important acoustic parameters such as acoustic impedance, adiabatic compressibility, free length, relaxation time, internal pressure, absorption coefficient, free volume, Rao's constant, Wada's constant, cohesive energy, Gibb's free energy, relative association and Van der Waal's constant were calculated. These parameters were used to study the molecular interactions in aqueous neomycin solutions. It was observed that the classical absorption and relaxation time decreases with the rise in temperature, due to weakening of intermolecular hydrogen bondings.

Keywords: Neomycin, Antibiotics, Acoustic parameters, Molecular interactions

INTRODUCTION

Neomycin is an aminoglycoside antibiotic. It is highly effective against Gram-positive and Gram-negative bacteria therefore it is commonly used for the prevention of bacterial contamination of cell cultures. The review of literature [1-5] revels that various acoustic parameters such as acoustic impedance, adiabatic compressibility, free length, relaxation time, internal pressure, absorption coefficient etc. are very useful for understanding the nature and strength of molecular interactions in liquid solutions. An excellent review on pharmacodynamics and pharmacokinetics of many antibiotics is reported by Campoli-Richards and Brogden [6]. However, a scanty work has been done on physico-chemical studies of antibiotics. In our previous study we have carried out studies on thermodynamic properties of streptomycin aqueous solutions [7]. In continuation of these investigations, in the present paper, we report ultrasonic velocity, density, viscosity and of aqueous Neomycin sulphate with different concentration range (0.0010 - 0.1003) mol kg⁻¹ at temperature T= (298.15, 303.15, 308.15) K. Using this data various acoustical parameters were determined and the results are interpreted in terms of molecular interactions in neomycin aqueous solutions.

MATERIALS AND METHODS

Neomycin sulphate, an aminoglycoside antibiotic (CAS No. 1405-10-3) having molecular weight of 908.90 was obtained from HIMEDIA Ltd. India. The experimental procedure adopted for the present investigation is similar to our previous work [7]. The solvent double distilled water was used to prepare the fresh solutions. All the solutions were prepared on molality (concentration) basis by using a monopan electric balance of least count 0.0001g. The densities of solvent and all freshly prepared solutions were measured by using hydrostatic sinker method at different temperatures T= (298.15, 303.15 and 308.15) K. While measuring the densities, the temperature of experimental liquid was maintained constant by using thermostat U-10. The uncertainty in the density measurements was \pm

0.0001 g/cm³. The speed of sound in aqueous solutions of the aminoglycoside antibiotic neomycin sulphate of different concentration at different temperatures were measured by using an ultrasonic interferometer specially designed for pulse- echo overlap technique, with a double walled liquid cell (2 MHz). The interferometer was calibrated by measuring the speed of sound in double distilled water. The viscosity of binary liquid solutions was measured by using Ostwald's viscometer owing to its versatility. The viscometer was placed in glass jar through which a current of water was maintained constant with the help of thermostat U-10. The jar was properly lagged by asbestos thread leaving suitable window to illuminate and observe the viscometer marks. The temperature of waterbath was maintained constant for a long time within an accuracy $\pm 0.1^{\circ}$ C. The time interval of crossing the liquid between two marks of the viscometer was measured by using an electronic digital timer ET-450A (ECIL). The accuracy of viscosity measurements was $\pm 0.1\%$.

Using above measured values, various thermodynamic parameters have been determined by using following empirical relations:

Acoustic impedance (Z)

 $Z = u\rho_s \tag{1}$

Adiabatic compressibility (β)

$$\beta = 1/u^2 \rho_s \tag{2}$$

Where u is ultrasonic velocity and ρ_s is the density of solution

Free length (L_f)

$$L_f = K_1 \beta^{1/2}$$
(3)

where K_1 is Jacobson, a temperature dependent constant $(K_1 = (93.875 + 0.375T) \times 10^{-8})$

Free Volume (V_f)

$$V_f = \left(M_{eff} u/k\eta\right)^{3/2} \tag{4}$$

where M_{eff} is effective molecular weight, η is viscosity and 'k' is constant equal to 4.28×10^9 independent of temperature for all types of liquids.

Internal pressure (π_i)

$$\pi_{i} = bRT \left(\frac{k\eta}{u}\right)^{\frac{1}{2}} \begin{pmatrix} \frac{\rho_{s}^{2}}{3} \\ \frac{\overline{\rho}_{s}}{M_{eff}^{7}} \end{pmatrix}$$
(5)

where *b* stands for the cubic packing factor which is assumed to be '2' for all liquids and solutions, *k* is temperature independent constant, *R* is gas constant and *T* is the absolute temperature. Relaxation time (τ)

$$\tau = 4/3\beta\eta \tag{6}$$

Absorption coefficient (α/f^2)

(

$$\alpha/f^2) = 8\pi^2 \eta/3\rho_s u^3 \tag{7}$$

Cohesive energy

$$C.E. = \pi_i \times V_f \tag{8}$$

Gibb's free energy (ΔG)

$$\Delta G = -kT \log(\frac{h}{\tau kT}) \tag{9}$$

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where k is the Boltzmann's constant $(1.23 \times 10^{-23} \text{J.K}^{-1})$, h the Planck's constant $(6.62 \times 10^{-34} \text{J.s})$

Relative association (R_A)

$$R_A = (\rho_s / \rho_0) \left(u_0 / u \right)^{\frac{1}{3}}$$
(10)

where ρ_s , u and ρ_0 , u_0 are respectively the density and ultrasonic velocity of the solution and solvent.

Rao's constant (R_a)

$$R_a = (M_{eff}/\rho_s) (u)^{\frac{1}{3}}$$
(11)

Molar compressibility or Wada's constant (W)

$$W = \left(\frac{M_{eff}}{\rho_s}\right) \beta^{-1/7} \tag{12}$$

Van der Waal's constant (b)

$$b = V_f \left(1 - \left(\frac{RT}{M_{eff} u^2} \right) \left(1 + \frac{M_{eff} u^2}{3RT} \right)^{1/2} \right)$$
(13)

RESULT AND DISCUSSION

Table 1: Experimental data of density, viscosity and ultrasonic velocity for Neomycin aqueous solutions at T= 298.15, 303.15 and 308.15 K

Danamatan	Temperature	Value of parameters measured for concentrations (mol.kg ⁻¹)					
rarameter	(K)	m=0.0010	0.0050	0.0100	0.0501	0.1003	
Density ps	298.15	0.9982	1.0004	1.0028	1.0148	1.0341	
10^3 (Kg.m ⁻³)	303.15	0.9970	0.9995	1.0015	1.0138	1.0333	
	308.15	0.9961	0.9976	0.9988	1.0113	1.0313	
Ultrasonic velocity	298.15	1498.11	1500.38	1503.58	1514.85	1528.36	
u (m.s ⁻¹)	303.15	1510.40	1512.82	1514.14	1526.89	1541.97	
	308.15	1519.08	1521.84	1524.07	1536.84	1552.71	
Viscosity η	298.15	0.908	0.975	0.995	1.099	1.213	
10^{-3} (N.s.m ⁻²)	303.15	0.816	0.884	0.905	0.998	1.096	
	308.15	0.738	0.782	0.794	0.862	0.931	

The observed values of densities, viscosities and ultrasonic velocities of aqueous neomycin solutions for different concentrations ranging from 0.0010 to 0.1003 mol kg⁻¹ at different temperatures T=(298.15, 303.15, 308.15) K are presented in Table 1. For systematic understanding the effect of concentration and temperature on these parameters, the graphs have been plotted and they are shown in Figs. 1 (a-c).

Fig. 1a shows that the density of the aqueous neomycin solution increases almost linearly with the rise in concentration and decreases with the rise in temperature which is a usual expected result. No abnormal change in density is observed. This indicates that the phenomenon of molecular aggregations do not affect the density of solution.

Fig. 1b represents the variation of viscosity with the rise in concentration of the understudied aqueous solution. It was found that with the increase in concentration, the viscosity increases sharply at first and then quite steadily for all temperatures. The effect of temperature was found to be decrease in viscosity of the solution. This effect is due to the increase in frictional resistance between the layers of medium which varies with the concentration and temperature.

The ultrasonic velocity variation in liquid gives the important information regarding the nature and the strength of molecular interaction. The change in ultrasonic velocity depends upon the change in elastic properties of the medium. Fig.1c suggests that the ultrasonic velocity increases with the rise in concentration for a given temperature. This is due to the increase in density and viscosity of the solution which leads to the decrease in compressibility of the solution. Smaller values of ultrasonic velocity at the beginning are due to weak solute-solvent interactions as the concentration is lower. With the increase in concentration, solute- solvent interaction increases and hence the ultrasonic velocity. The linear behavior of ultrasonic velocity at later stage also indicates that there is no complex formation in the system. The similar investigations are reported [8-11] for various aqueous drug solutions.



Fig. 1 Effect of Concentration and Temperature on (a) Density, (b) Viscosity, and (c) Ultrasonic velocity of aqueous neomycin solutions

Table 2: Derived parameters of Neomycin aqueous solutions at T= (298	3.15, 303.15, 308.15) K

Parameter	T (K)	Value of narameters obtained for concentrations (mol $k\sigma^{-1}$)				
i urumeter	1 (11)	m=0.0010	0.0050	0.0100	0.0501	0.1003
Acoustic impedance Z 10^6 (Kg. m ⁻² .s ⁻¹)	298.15	1.495	1.500	1.507	1.537	1.580
	303.15	1.505	1.512	1.516	1.548	1.593
	308.15	1.513	1.518	1.522	1.554	1.601
Adiabatic compressibility β						
$10^{-10} (N^{-1}m^2)$	298.15	4.464	4.440	4.411	4.294	4.140
	303.15	4.397	4.372	4.355	4.231	4.070
Free length L_f 10^{-11} (m)	308.15	4.350	4.328	4.310	4.187	4.022
	298.15	4.346	4.335	4.320	4.263	4.185
	303.15	4.353	4.341	4.332	4.270	4.188
Free volume V_f 10 ⁻⁸ (m ³ mol ⁻¹)	308.15	4.368	4.356	4.347	4.285	4.199
	298.15	1.830	1.658	1.624	1.491	1.387
	303.15	2.175	1.944	1.892	1.744	1.637
Internal pressure $\pi_i 10^9$ (Pa)	308.15	2.550	2.357	2.325	2.194	2.113
	298.15	2.734	2.823	2.839	2.876	2.902
	303.15	2.623	2.721	2.741	2.773	2.791
Relaxation time $\tau = 10^{-13}$ (s)	308.15	2.526	2.590	2.597	2.607	2.602
	298.15	5.404	5.773	5.852	6.292	6.696
	303.15	4.784	5.153	5.255	5.630	5.948
Absorption coefficient $\alpha/f^2 = 10^{-15}$	308.15	4.281	4.513	4.563	4.812	4.993
	298.15	7.113	7.587	7.675	8.191	8.639
Cohesive energy	303.15	6.245	6.716	6.844	7.271	7.606
$(J mol^{-1})$	308.15	5.557	5.848	5.904	6.174	6.340
	298.15	50.043	46.000	46.098	42.885	40.247
Gibb's free	303.15	57.038	52.887	51.849	48.368	45.672
Energy 10^{-21} (J mol ⁻¹)	308.15	64.436	61.056	60.358	57.200	54.965
	298.15	4.022	4.264	4.314	4.580	4.808
Relative	303.15	3.696	3.974	4.047	4.304	4.509
Association(R_A)	308.15	3.399	3.599	3.641	3.842	3.982
	298.15	0.9982	0.9999	1.0016	1.0110	1.0272
	303.15	1.0010	1.0030	1.0047	1.0142	1.0304
	308.15	1.0020	1.0029	1.0036	1.0133	1.0298





Fig. 2 Variations of various derived parameters with concentration (a) Acoustic inpedence, (b) Adiabatic compressibility, (c) Free length, (d) Free volume, (e)Internal pressure, (f) Relaxation Time, (g) Absorption coefficient, (h) Cohesive energy, and (i) Gibb's free energy of aqueous neomycin solutions at different temperatures

Table 2 shows various acoustic parameters which were determined form the measured parameters, i.e, ultrasonic velocity, density, and viscosity.

The component of the solution that resists the ultrasonic wave propagation is known as acoustic impedance. Fig.2a shows the variation of acoustic impedance with concentration, and temperature. The increase in acoustic impedance with the increase in concentration as well as temperature in the present aqueous solution is due to the change in inertial properties and elastic properties of the solution. This indicates the molecular association of solute and solvent through the hydrogen bonding.

Physico-chemical properties of liquid can be understood by adiabatic compressibility as the hydrogen bonding between the unlike components in the solutions decreases with the compressibility [12, 13]. The addition of solute makes the medium denser due to which the adiabatic compressibility decreases with the concentration. The compressibility also decreases with the temperature. These characteristics are found to be valid in the present case as the behavior of the adiabatic compressibility shown in Fig. 2b follow the same nature.

The variation of free length is shown in Fig.2c. It is observed from this figure that the free length of aqueous neomycin solution decreases with the rise in concentration. This indicates that there exists a significant solute-solvent interaction which leads to a structure promoting behavior. The decreasing trend of free length with rise in concentration is due to decrease in spacing between the molecules of aqueous neomycin solution. The free length however, was found to be increases with the rise in temperature as higher temperature increases the spacing between the molecules. This type of variation in the free length is due to the presence of dipole-dipole interaction and donar-acceptor interactions between solute solvent molecules; it also indicates structure promoting tendency of solute [14-16].

Fig. 2d shows the variation of free volume of aqueous neomycin solution with concentration and also with the temperature. Structure making or breaking nature of water with salt can be understood by the free volume [17]. The decrease in free volume with the rise in concentration and with the rise in temperature confirms the presence of ion-solvent interactions [18]. The decrease in free volume with the concentration of the solution shows that the spacing

between the solute and solvent molecule decreases as a consequence of which there is strengthening of solute-solvent interaction.

Many researchers reported the significance of internal pressure and its correlation with various thermodynamic parameters [19-21]. Internal pressure of the solution which is measure of cohesive force between the molecules is found to be decreased with rise in temperature as shown in Fig. 2e. The nature of internal pressure with the rise in temperature is due to solute-solvent interactions.

The relaxation time variation of aqueous neomycin solutions at different temperature is as shown in Fig.2f. This figure shows that the relaxation time increases with the concentration, and decreases with the temperature. This effect is due to weakening of intermolecular hydrogen bonding and structure breaking effect caused by thermal vibrations [22].

The classical absorption value of aqueous neomycin solution increases with the concentration and decreases with the temperature as shown in Fig.2g, strongly supports the intermolecular hydrogen bonding and enhanced solute solvent interactions [23]. The close packed water structure absorbs more sound energy due to intermolecular hydrogen bonding and hence more the classical absorption value.

Variations in cohesive energy and Gibbs free energy with concentration and temperature are shown in Fig. 2h and Fig. 2i respectively. They show vice-versa characteristics. These observations are agreed with the reported literature [24, 4].

Relative association is the important property by which the firm impact of molecular interactions can be understood. In the present study relative association of aqueous solution is increased with rise in concentration shows that this property is influenced by salvation of solute molecule [25]. Increase in relative association with concentration shows increase in solute-solvent interactions [26]

Constants	Temperature	e Value of constants obtained for concentrations (
	(K)	m=0.0010	0.0050	0.0100	0.0501	0.1003
Rao's constant R _a	298.15	2.065	2.069	2.075	2.129	2.184
$10^{-4} (m^5 N^{-1})$	303.15	2.073	2.077	2.082	2.137	2.192
	308.15	2.079	2.085	2.093	2.147	2.202
Wada's constant W	298.15	3.910	3.919	3.930	4.039	4.152
$10^{-4} (m^4 s^{-1})$	303.15	3.923	3.931	3.943	4.052	4.166
	308.15	3.933	3.944	3.959	4.068	4.182
Van der Waal's constant 10 ⁻⁵ cm ³ mole ⁻¹	298.15	1.524	1.527	1.532	1.576	1.622
	303.15	1.526	1.529	1.533	1.578	1.623
	308.15	1.527	1.531	1.537	1.581	1.626

Table 1: Derived Parameters for Neomycin aqueous solutions at T= (298.15, 303.15, 308.15) K

Table 3 shows some constants such as Rao constant, Wada Constant and Van der Waal constant for various concentration of the solution at different temperatures. Rao constant is a measure of extent of interaction existing in solution. The values of Rao constant shows increasing trend with the concentration indicates that the magnitude of interactions is enhanced. Wada constant depends on adiabatic compressibility and is taken as confirmation for existing interactions. The increasing trend in Wada constant with concentration indicates the presence of large number of solute-solvent molecules in a given region, thus leads to tight packing of the medium and enhanced molecular interactions [27].

CONCLUSION

Ultrasonic velocity, density and viscosity of aqueous neomycin solution were measured for different concentrations and temperatures. Other important acoustic parameters were calculated. These parameters were interpreted in connection with the molecular interactions in aqueous neomycin solution. In general we found that the molecular interaction increases with the addition of neomycin solute in water. The temperature effect on these parameters was also discussed at appropriately.

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