

Acoustical and Thermodynamic Properties of Some Antibiotic Drugs at 2 MHz by Ultrasonic Interferometry- A Comparative Study

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Abstract: Density, viscosity and ultrasonic velocity measured experimentally for the aqueous solutions of ceftriaxone sodium, cefotaxime sodium and ampicillin sodium with different concentrations and temperature and 2MHz frequency. Acoustical and thermodynamic parameters such as Wada's constant, Rao's constant, relative association, specific acoustic relaxation time, free volume, adiabatic compressibility, intermolecular free length, specific acoustic impedance and apparent molar volume determine from experimental data. The results have been interpreted to comparative study of molecular interactions in the aqueous solution of Ceftriaxone sodium, Ampicillin sodium and Cefotaxime sodium.

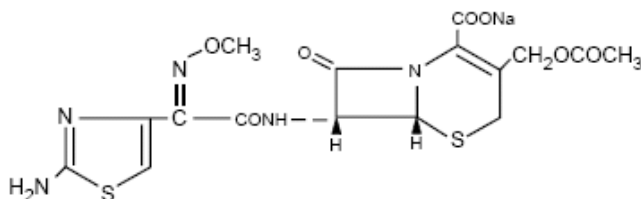
Keywords: ceftriaxone sodium; cefotaxime sodium; ampicillin sodium; acoustical thermodynamic parameters; molecular interaction

I. INTRODUCTION

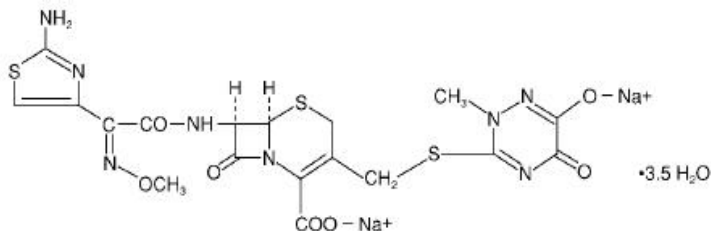
The binding forces between the atoms or the molecules in liquid is related to ultrasonic velocity. Measurement of ultrasonic velocity gives information about physico-chemical behavior of solutions and liquid mixtures and molecular interactions of multi-component liquid mixtures. Ultrasound has been extensively used in various medical applications, including medical diagnostic imaging and physiotherapeutic treatment and can be considered safe for use in patients. Molecular interaction in aqueous solution of different antibiotics by number of researchers¹⁻¹⁵. In pharmaceuticals Ampicillin sodium, Cefotaxime sodium and Ceftriaxone sodium is used as an antibiotics.

In the present work, different antibiotics were studied at different concentration, temperature and frequency at 2MHz in comparative manner. In aqueous solutions of different antibiotics, solute-solvent interaction have been interpreted by using acoustic and thermodynamic parameters like adiabatic compressibility, intermolecular free length, specific acoustic impedance, wada's constant, rao's constant, relative association, specific acoustic relaxation time, free volume and apparent molar volume.

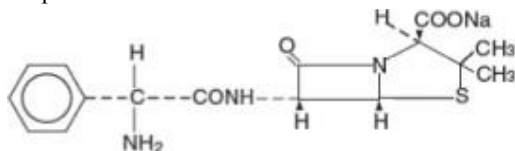
Cefotaxime sodium -



Ceftriaxone sodium -



Ampicillin sodium-



Experimental:

Different antibiotics such as Ampicillin sodium manufactured by Aristo Pharmaceuticals Private Limited, Cefotaxime sodium manufactured by Alkem laboratories Limited and ceftriaxone sodium manufactured by Prosperity 6 pharmaceuticals Limited was used. All the chemicals used were of analytical grade. Solutions were prepared by double distilled water. Ultrasonic sound velocities of various solutions were measured in Multi frequency interferometer operating at 2MHz frequency supplied by Mittal Enterprises, India; Model F-83 with accuracy of $\pm 0.03\%$ was used. Densities of various solutions were determined using 10 ml specific gravity bottle with accuracy of $\pm 0.1 \text{ kg/m}^3$. Digitally control and well-stirred special thermostatic water bath with an accuracy of $\pm 0.1^\circ\text{C}$ was used for measurement of density and ultrasonic velocity. Digital electronic balance CA-124 (CB/CA/CT series, Contech) with accuracy of $\pm 0.0001 \text{ g}$ was used for weighing.

Result and discussion:

Ultrasonic velocities, viscosity and densities of water and aqueous solution of ampicillin sodium, cefotaxime sodium and ceftriaxone sodium were measured.

The adiabatic compressibility (β) is determined by formula,

$$\beta = 1 / v^2 \cdot d \quad \dots \dots (1)$$

Specific acoustic impedance is determined by formula,

$$Z = v_s \cdot d_s \quad \dots \dots (2)$$

Intermolecular free length is determined by Jacobson's formula,

$$L_f = K \sqrt{\beta_s} \quad \dots \dots (3)$$

Where, K is Jacobson's constant independent of the nature of liquid. (At 303.15 K, K=631).

Rao's constant is determined by formula.

$$R = [M_{\text{eff}}/d_s] v^{1/3} \quad \dots \dots (4)$$

Wada's constant is determined by formula.

$$W = [M_{\text{eff}}/d_s] \beta^{-1/7} \quad \dots \dots (5)$$

Relative association is measured by following equation as

$$R_A = \frac{d_s}{d_0} \left(\frac{v_0^{1/3}}{v_s} \right) \quad \dots \dots (6)$$

Where, v_0 and v_s are ultrasonic velocities in solvent and solution respectively



Specific acoustic relaxation time is measured by equation

$$T = 4/3\beta \cdot \eta \dots \dots (7)$$

Apparent molar volume is measured by following equation

$$\Phi_v = 1000(d_0 - ds) / (cds + d_0 + M/ds) \dots \dots (8)$$

Where, c is the molality of the solution, M is the molecular weight of solute.

Free volume is measured by following following equation

$$V_f = [M_{eff} / K \eta]^{3/2} \dots \dots (9)$$

Where, M_{eff} is effective molecular weight, K is a temperature independent constant which is equal to 4.28×10^9 for all liquids.

Viscosity is measured by following equation

$$\eta_2 = \eta_1 \cdot t_2 \cdot ds / t_1 \cdot d_0 \dots \dots (10)$$

Where, η_1 = viscosity of water, η_2 = viscosity of experimental liquid, t_1 = time flow of water, t_2 = time flow of experimental liquid, d_0 = density of water and ds = density of experimental liquid.

Values of ultrasonic velocity, viscosity density, adiabatic compressibility, intermolecular free length, specific acoustic impedance, wada's constant, rao's constant, relative association, specific acoustic relaxation time, free volume and apparent molar volume of aqueous solution of ampicillin sodium, cefotaxime sodium and ceftriaxone sodium at different concentrations, temperatures and at 2MHz frequency are shown in table 1A, 1B, 2A, 2B and 3A, 3B respectively.

Table 1A: Acoustic parameters of aqueous solution of Ampicillin sodium at 2MHz

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Adiabatic compressibility $\beta \times 10^{10}$	Specific acoustic impedance $Z \times 10^4$ (Kg m ⁻² sec ⁻¹)	Intermolecular free length L_f (Å ⁰)	Rao's constant	Wada's constant
303.15	0.001	1456.63	1024.94	4.59	14.9295	0.0134	0.1991	0.3790
	0.01	1528.85	1028.97	4.15	15.7314	0.0127	0.2023	0.3844
	0.1	1598.42	1033.77	3.78	16.5239	0.0122	0.2123	0.4027
308.15	0.001	1526.69	1019.55	4.21	15.5653	0.0129	0.2033	0.3858
	0.01	1526.79	1022.23	4.20	15.6073	0.0129	0.2036	0.3865
	0.1	1598.55	1027.55	3.18	16.4259	0.0123	0.2136	0.4048
313.15	0.001	1492.82	1017.30	4.41	15.1864	0.0133	0.2023	0.3841
	0.01	1563.28	1018.65	4.02	15.9243	0.0127	0.2059	0.3903
	0.1	1601.06	1025.79	3.80	16.4235	0.0129	0.2140	0.4056

Table 1B: Acoustic parameters of aqueous solution of Ampicillin sodium at 2MHz

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Viscosity $\eta \times 10^3$ (NSm ⁻²)	Acoustic relaxation time $T \times 10^{-10}$ (sec)	Relative association n (R_A)	Free Volume $V_f \times 10^{-8}$ (m ³ /mole)	Apparent molar volume
303.15	0.001	1456.63	1024.94	0.8514	5.2203	1.0390	1.1920	-28.6
	0.01	1528.85	1028.97	0.8896	4.9321	1.0264	1.3770	-2.92
	0.1	1598.42	1033.77	0.9639	4.8660	1.0160	1.7567	-0.014
308.15	0.001	1526.69	1019.55	0.7252	4.0695	1.0278	1.0100	-24.5
	0.01	1526.79	1022.23	0.7517	4.2061	1.0304	1.0700	-2.38



	0.1	1598.55	1027.55	0.8049	4.0872	1.0201	1.3400	0.05
313.15	0.001	1492.82	1017.30	0.6651	3.9122	1.0340	0.8540	-23.4
	0.01	1563.28	1018.65	0.6821	3.6534	1.0196	0.9560	-2.15
	0.1	1601.06	1025.79	0.7353	3.7289	1.0186	1.1700	0.042

Table 2A: Acoustic parameters of aqueous solution of Cefotaxime sodium at 2MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Adiabatic compressibility $\beta \times 10^{-10}$	Specific Acoustic Impedance $Z \times 10^4$ (Kg m ⁻² sec ⁻¹)	Intermolecular free length L_r (Å ⁰)	Rao's constant	Wada's constant
303.15	0.001	1489.33	1016.16	4.43	15.1339	0.01320	0.2023	0.3842
	0.01	1491.21	1025.55	4.38	15.2921	0.01313	0.2013	0.3828
	0.1	1524.10	1043.55	4.12	15.9047	0.01273	0.2071	0.3943
308.15	0.001	1526.54	1006.14	4.27	15.3591	0.01294	0.2060	0.3902
	0.01	1527.13	1016.52	4.22	15.5235	0.01287	0.2048	0.884
	0.1	1564.90	1039.00	3.93	16.2593	0.01243	0.2098	0.3988
313.15	0.001	1563.38	999.53	4.09	15.6264	0.01268	0.2091	0.3951
	0.01	1528.29	1010.52	4.24	15.4436	0.01290	0.2060	0.3904
	0.1	1637.99	1038.66	3.59	17.0131	0.01187	0.2131	0.4041

Table 2B: Acoustic parameters of aqueous solution of Cefotaxime sodium at 2MHz

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Viscosity $\eta \times 10^3$ (NSm ⁻²)	Specific relaxation time $\tau \times 10^{-10}$ (sec)	Relative association (R_A)	Free Volume $V_f \times 10^{-8}$ (m ³ /mole)	Apparent molar volume
303.15	0.001	1489.33	1016.16	0.8699	5.13	1.0225	1.27	-20.15
	0.01	1491.21	1025.55	0.9301	4.19	1.0315	1.41	-2.49
	0.1	1524.10	1043.55	1.1765	6.46	1.0420	2.20	-0.007
308.15	0.001	1526.54	1006.14	0.9168	4.32	1.0143	1.43	-11.36
	0.01	1527.13	1016.52	0.9262	5.50	1.0246	1.46	-1.72
	0.1	1564.90	1039.00	0.9467	5.26	1.0388	1.66	0.026
313.15	0.001	1563.38	999.53	0.7559	3.85	1.0004	1.11	-5.89
	0.01	1528.29	1010.52	0.7642	4.12	1.0191	1.10	-1.25
	0.1	1637.99	1038.66	0.7855	4.05	1.0235	1.34	-0.029

Table 3A: Acoustic parameters of aqueous solution of Ceftriaxonesodium at 2MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Adiabatic compressibility $\beta \times 10^{-10}$	Specific acoustic impedance $Z \times 10^4$ (Kg m ⁻² sec ⁻¹)	Intermolecular free length L_r (Å ⁰)	Rao's constant	Wada's constant
303.15	0.001	1488.09	1025.40	4.40	15.2588	0.0131	0.2004	0.3812



308.15	0.01	1488.34	1030.70	4.37	15.3403	0.0131	0.2002	0.3810
	0.1	1489.44	1054.37	4.27	15.7041	0.0129	0.2035	0.3884
	0.001	1524.32	1020.93	4.22	15.3622	0.0129	0.2029	0.3852
	0.01	1525.20	1026.42	4.19	15.6549	0.0129	0.2027	0.3850
	0.1	1525.49	1044.61	4.11	15.9354	0.0128	0.2070	0.3942
313.15	0.001	1554.55	1015.52	4.07	15.7867	0.0128	0.2054	0.3892
	0.01	1563.54	1016.94	4.02	15.9002	0.0127	0.2063	0.3909
	0.1	1598.64	1038.52	3.77	16.6022	0.0123	0.2115	0.4016

Table 3B: Acoustic parameters of aqueous solution of Ceftriaxonesodium at 2MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m ³)	Viscosity $\eta \times 10^3$ (NSm ⁻²)	Specific relaxation time $\tau \times 10^{-10}$ (sec)	Relative association (R_A)	Free Volume $V_f \times 10^{-8}$ (m ³ /mole)	Apparent molar volume
303.15	0.001	1488.09	1025.40	0.8431	4.9508	1.0321	1.2128	-28.8
	0.01	1488.34	1030.70	0.8736	5.1022	1.0374	1.2873	-2.8
	0.1	1489.44	1054.37	1.1529	6.5722	1.0609	2.0700	0.064
308.15	0.001	1524.32	1020.93	0.7507	4.2197	1.0297	1.0600	-25.5
	0.01	1525.20	1026.42	0.7794	4.3523	1.0350	1.1300	-2.2
	0.1	1525.49	1044.61	1.0019	5.4956	1.0533	1.7400	0.148
313.15	0.001	1554.55	1015.52	0.6720	3.6511	1.0183	0.9220	-21.4
	0.01	1563.54	1016.94	0.7208	3.8670	1.0178	1.0400	-1.69
	0.1	1598.64	1038.52	0.8508	4.2745	1.0317	1.4600	0.197

Table 1A and 1B reveals that at 2MHz frequency, ultrasonic velocity of aqueous solution of ampicillin sodium increases with increase of concentration and same is non-linear with increase of temperature indicates maximum association among the molecules of aqueous ampicillin sodium solution due to effective solute-solvent interaction. With increase of concentration, adiabatic compressibility and intermolecular free length decreases whereas non-linear with increase of temperature indicates enhanced molecular association and favors structure promoting nature of solute molecules of ampicillin sodium. Specific acoustic impedance increases with increase of concentration and variation with increase of temperature indicates associative molecular interactions in aqueous ampicillin sodium solution. Values of Rao's constant increase with increase in concentration and temperature indicates that magnitude of molecular interaction enhanced in aqueous solution of ampicillin sodium. Values of Wada's constant increase with increase in concentration and temperature indicates strong solute-solvent interaction in aqueous solution of ampicillin sodium. This observation is similar to that of S. Baluja et al¹⁶. Relative association is non-linear with increase of concentration and temperature indicates specific molecular interactions among the components. Relaxation time decreases with increase in temperature and increases with increase of concentration indicate presence of specific molecular interaction among ampicillin sodium and water. Free volume increases with increase in concentration suggest structure breaking nature whereas same decreases with increase in temperature suggest structure promoting nature. Apparent molar volume increases with increase in concentration and temperature. Values of Φ_v are negative except for 0.1M at 313.15K, it is positive. Negative values of Φ_v indicate compactness of medium and after dissolution of solute due to close packing of molecules inside the shell more clinging is occurring. Value of apparent molar volume is positive for 0.1M at 313.15K. This indicates that molecular interactions are maximum for 0.1M at 313.15K.

Table 2A and 2B reveals that at 2MHz frequency, density and viscosity of aqueous solution of cefotaxime sodium increase with increase in concentration and with increase of temperature same decreases. With increase in temperature density decreases shows intermolecular forces decreases due to increase of thermal energy. Ultrasonic velocity increases



with increases in temperature and concentration. Increase of ultrasonic velocity and density indicates moderate attraction among the solute and solvent molecules of aqueous solution of cefotaxime sodium. With increase in concentration and temperature, value of adiabatic compressibility decreases indicate close packing and clinging of molecules shows strong intermolecular association between the solute and solvent molecules of aqueous solution of cefotaxime sodium due to hydrogen bond formation. With increases of temperature and concentration intermolecular free length decreases indicates breaking of dipole in cefotaxime sodium shows structure promoting behavior of solute molecule of cefotaxime sodium. Specific acoustic impedance increases with increases concentration and temperature indicates molecular packing in medium increase shows molecular interaction enhances in aqueous solution of cefotaxime sodium. Rao's constant increase with increase in temperature and same decreases up to 0.01M concentration further it increases with increase in concentration. The increasing trends of molar sound velocity with increasing concentration and temperature indicates the more number of components in the given region, thus leads to tight packing of the medium and thereby increase the magnitude of interaction. Wada's constant increase with increase in temperature and same decreases up to 0.01M concentration further it increases with increase in concentration indicates the strengthening of interaction in aqueous solution of cefotaxime sodium. Same results are observed in Nithiyantham et al¹⁷. Relaxation time and relative association increases with increase in concentration and same decreases with rise in temperature reflects strong intermolecular interaction between molecules of solute cefotaxime sodium and solvent water. Value of Free volume of aqueous solution of cefotaxime sodium increases with increases concentration and temperature indicates strong of molecular interaction. Values of apparent molar volume increases with increase in concentration and temperature, this suggests existence of ion-solvent interaction. Negative values of Φ_v indicate compactness of medium and after dissolution of solute due to close packing of molecules inside the shell more clinging is occurring. It further supports electrostrictive solvation of ions¹⁸.

Table 3A and 3B reveals that at 2MHz frequency, ultrasonic velocity of aqueous solution of ceftriaxone sodium increases with increases in concentration and temperature indicates molecular association greater due to solute-solvent interaction and cohesion brought by the ionic hydration. With increase in concentration and temperature, adiabatic compressibility decreases indicates formation of hydrogen bonding which gives close packed structure result existence of strong solute-solvent interaction in aqueous solution of ceftriaxone sodium. With increase of concentration and temperature, decreases intermolecular free length indicates structure promoting behavior of solute molecule ceftriaxone sodium. Specific acoustic impedance increases with increases concentration and temperature indicates molecular packing increase in the medium support molecular interaction due to hydrogen bonding. It can be easily seen that the values of Rao's constant increase with increase in temperature whereas non-linear behavior with concentration. Increase of Rao's constant with increase in temperature indicates that availability of more number of solute molecules in a given region this leads to a tight packing of medium suggests strong interaction existing in aqueous solution of ceftriaxone sodium. Wada's constant increase with increase in temperature whereas non-linear behavior with concentration that is it decreases up to 0.01M further it increases with increase in concentration at 303.15K and 308.15K temperature except at 313.15K, it increases linearly with increase in concentration As concentration increases relaxation time, relative association and free volume increases whereas as temperature increases same decreases shows in aqueous solution of ceftriaxone sodium presence of specific molecular interaction. With increase in concentration and temperature values of apparent molar volume increases. Negative values at 0.001M and 0.01M suggest ionic and hydrophilic interaction occurring in the solution. Interaction is of ion-solvent type. Apparent molar volume is highest at 0.1M for 313.15K. This suggests that molecular interactions are maximum at 0.1M for 313.15K.

II. CONCLUSION

On comparing the trends of acoustic and thermodynamic parameters of aqueous solution of ampicillin sodium, cefotaxime sodium and ceftriaxone sodium, Trends of acoustic and thermodynamic parameters of aqueous solution of ampicillin sodium, cefotaxime sodium and ceftriaxone sodium favors strong intermolecular interaction in ampicillin sodium solution than cefotaxime sodium and ceftriaxone sodium. This observation may conclude that ampicillin sodium may be thought as more powerful and potent antibiotic than other two drugs cefotaxime sodium and ceftriaxone sodium.



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