RELATIVE ASSOCIATION, SPECIFIC ACOUSTIC IMPEDANCE AND FREE VOLUME OF ANTIBIOTIC CEFOTAXIME SODIUM

Rajesh S. Hajare[1], Sunanda S. Aswale[2]and Shashikant R. Aswale[2]
[1]Nilkanthrao Shinde College, Bhadrawati, Dist. Chandrapur, Maharashtra, India
[2]Lokmanya Tilak Mahavidyalaya, Wani, Dist. Yavatmal, (MS), India

A B S T R A C T

The study of intermolecular interaction plays important role in development of molecular sciences. Among the non-spectroscopic methods in the study of molecular interaction, the ultrasonic measurement finds extensive applications owing to its ability of characterizing the physico-chemical behavior of the liquid systems from data. The ultrasonic velocity of liquid is fundamentally related to the binding forces between the atoms or molecules. Ultrasonic parameters provide valuable information about various inter and intramolecular interactions in solutions. Cefotaxime sodium is used as an antibiotic in pharmaceutical. It is antibacterial, β-lactum; third generation cephalosporin. Ultrasonic velocity, density and viscosity of aqueous solution of cefotaxime sodium at different concentrations, temperatures and different frequencies such as 2, 4 and 6 MHz have been experimentally determined. Ultrasonic parameters such as relative association and specific acoustic impedance of these solutions are calculated on the basis of these measurements. Various molecular interactions in these solutions have been analyzed on the basis of the variation of these parameters with concentration, temperature and frequency.

Keywords: ultrasonic velocity, acoustical parameters, molecular interactions, cefotaxime sodium

1. Main text

Here introduce the paper, and put a nome-nclature if necessary, in a box with the same font size as the rest of the paper. The paragraphs continue from here and are only separated by headings, subheadings, images and formulae. The section headings are arranged by numbers, bold and 9.5 pt. Here follows further instructions for authors.

1. Introduction

The structure, nature and prevailing conditions of solvents and solutes play an important role on resulting properties and interactions occurring in solutions. According to physical concept of liquid model, molecules in the liquid states are loosely packed as to leave some free space in between them. The intermolecular free space and its dependant properties are related to intermolecular interactions and may reveal some information regarding the interaction, which may be occurring when liquids are mixed together. Acoustical and thermodynamic properties are of great significance in studying the physico-chemical behavior and molecular interactions in pure liquid components and their mixture. Literature survey shows that ultrasonic study of liquid mixture is highly useful in understanding the nature of molecular interactions[1-4] and physico-chemical behavior of liquid mixtures. A number of researchers[1-4] has investigated the molecular interaction in aqueous solution of different antibiotics. Cefotaxime sodium is used as an antibiotic in pharmaceuticals.

In continuation of our work [5-21] in the present study, ultrasonic velocity, density and viscosity measurement of aqueous solution of antibiotic cefotaxime sodium at different temperatures, concentrations and frequencies was carried out. The data obtained is used to calculate various acoustical parameters. The data and the results obtained during this investigation may give detail information regarding molecular interactions, drug absorption and transmission activity. Taking all

these things in consideration, this research work was carried out.

2. Experimental:

Antibiotic drug cefotaxime sodium obtained from Alkem laboratories limited was used. Double distilled water was used for making solutions. Densities were measured with the help of density bottle. Weighing was done on CB/CA/CC Conpech Digital Balance CCB-124, (± 0.0001 g). A special thermostatic water bath arrangement for constant temperature was made for density, viscosity and ultrasonic velocity measurements in which there is continuous stirring of water with the help of electric stirrer and temperature variation was maintained within ± 0.1°C. All the ultrasonic velocities were measured by multi frequency interferometer (Mittal Enterprises, Model F-83) with accuracy of ± 0.03% at frequencies 2MHz, 4MHz and 6MHz. Viscosities of the solutions were measured by Oswald's viscometer.

3. Results and Discussion

In the present investigation, measurements of densities, viscosities and ultrasonic velocities of solvent water and an antibiotic cefotaxime sodium solution in water have been made.
Specific acoustic impedance is determined from equations,

$$Z = v_s.d_s \quad (1)$$

Relative association is a function of ultrasonic velocity and is calculated by the equation,

$$R_A = \frac{d_s}{d_0}\left(\frac{v_0}{v_s}\right)^{1/3} \quad (2)$$

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

Free volume is calculated by following equation

$$V_f = [Meffv/K\eta]^{3/2} \quad (3)$$

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 of Solution is calculated by equation

$$\eta_2 = \eta_1.t_2.ds/t_1.d_0 \quad \ldots\ldots (4)$$

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.

The values of ultrasonic velocities, densities, viscosities, relative association and specific acoustic impedance at different frequencies, concentrations and temperatures are tabulated in table 1, 2 and 3.

Table 1 Acoustic parameters of aqueous solution of Cefotaxime sodium at 2MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Specific Acoustic Impedance $Zx10^4$ ($Kgm^{-2}sec^{-1}$)	Relative association (R_A)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1489.33	1016.16	0.8699	15.1339	1.0225	1.27
	0.01	1491.21	1025.55	0.9301	15.2921	1.0315	1.41
	0.1	1524.10	1043.55	1.1765	15.9047	1.0420	2.20
308.15	0.001	1526.54	1006.14	0.9168	15.3591	1.0143	1.43
	0.01	1527.13	1016.52	0.9262	15.5235	1.0246	1.46
	0.1	1564.90	1039.00	0.9467	16.2593	1.0388	1.66
313.15	0.001	1563.38	999.53	0.7559	15.6264	1.0004	1.11
	0.01	1528.29	1010.52	0.7642	15.4436	1.0191	1.10
	0.1	1637.99	1038.66	0.7855	17.0131	1.0235	1.34

Table 2 Acoustic parameters of aqueous solution of Cefotaxime sodium at 4MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Specific Acoustic Impedance $Zx10^4$ ($Kgm^{-2}sec^{-1}$)	Relative association (R_A)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1525.52	1016.16	0.8699	15.5017	1.0387	1.31
	0.01	1523.95	1025.55	0.9301	15.6288	1.0487	1.46
	0.1	1527.27	1043.55	1.1765	15.9378	1.0663	2.21
308.15	0.001	1599.44	1006.14	0.9168	16.0926	1.0179	1.53
	0.01	1593.29	1016.52	0.9262	16.1961	1.0297	1.56
	0.1	1599.81	1039.00	0.9467	16.6220	1.0511	1.71
313.15	0.001	1596.21	999.53	0.7559	15.9546	1.0254	1.14
	0.01	1597.07	1010.52	0.7642	16.1307	1.0366	1.17
	0.1	1672.37	1038.66	0.7855	17.3702	1.0493	1.38

Table 3 Acoustic parameters of aqueous solution of Cefotaxime sodium at 6MHz**.**

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Specific Acoustic Impedance $Zx10^4$ ($Kgm^{-2}sec^{-1}$)	Relative association (R_A)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1633.63	1016.16	0.8699	16.6002	1.0227	1.46
	0.01	1643.56	1025.55	0.9301	16.8555	1.0301	1.64
	0.1	1636.14	1043.55	1.1765	17.0739	1.0497	2.45
308.15	0.001	1635.60	1006.14	0.9168	16.4564	1.0346	1.58
	0.01	1638.54	1016.52	0.9262	16.6560	1.0446	1.62
	0.1	1639.92	1039.00	0.9467	17.0387	1.0674	1.78
313.15	0.001	1640.79	999.53	0.7559	16.5001	1.0272	1.19
	0.01	1643.10	1010.52	0.7642	16.6038	1.0401	1.22
	0.1	1738.32	1038.66	0.7855	18.0552	1.0492	1.47

From the experimentally determined values of density, viscosity and ultrasonic velocity of aqueous solution of cefotaxime sodium at different concentrations, temperatures and at different frequencies such as 2MHz, 4MHz and 6MHz, various acoustical parameters like relative association, specific acoustic impedance and free volume have been evaluated and presented in the Table-1,2 and 3. From this data molecular interaction in aqueous solution of cefotaxime sodium will be predicted.

A minute observation of the Tables 1, 2 and 3 suggest that the experimentally calculated values of ultrasonic velocity of aqueous solution of cefotaxime sodium increases with increases in concentration, temperature as well as frequency such as 2MHz, 4MHz and 6MHz where as the values of density and viscosity increase with increase in concentration and the same deceases with increase of temperature. The increasing values of density, viscosity and ultrasonic velocity show that there is moderate attraction between solute and solvent molecules. The decrease in values of density and viscosity with increase in temperature shows decrease in intermolecular forces due to increasing the thermal energy of the system.

Relative association is the measure of extent of association of components in the medium. Relative association is a property of understanding the interaction[22] which is influenced by two factors:-

1) Breaking of solvent structure on addition of solute to it and
2) Solution of solute, those are simultaneously present, by the free solvent molecules.

The former effect result in decrease in R_A values while latter resulting in increase of R_A values

From table 1, 2 and 3, it can be easily seen that the R_A values increase with increase in concentration and frequency and same decreases with rise in temperature, which is reverse trend that is observed for adiabatic compressibility. Increase in R_A with increase in concentration and frequency; suggests that salvation of solute is predominant over the breaking of solvent structure whereas, decrease in R_A with increase in temperature suggests that breaking of solvent structure is predominant over the solution of solute due to polar nature of water. This supports the strengthening of interaction among Cefotaxime sodium and water molecules due to formation of hydrogen bond between Cefotaxime sodium and water molecule.

Specific acoustic impedance is the impedance offered to the sound wave by the components of mixture. Specific acoustic impedance also makes the contribution in explaining molecular interactions. The mathematical relation for Specific acoustic impedance and adiabatic compressibility shows that their behavior is opposite. The conventional approach based on compressibility is both useful and fundamental; however acoustic impedance constitutes an additional probe for studding molecular interactions. Specific acoustic impedance is the complex ratio of the effective sound pressure at a point to the effective particle velocity at that point.[23]

It can be seen from table 1, 2 and 3, that the values of acoustic impedance increases with increase in of concentration, temperature and frequency, which is reverse to that of adiabatic compressibility. This suggests increase in molecular packing in medium and also supports strengthening of molecular interaction among the components of aqueous solution of Cefotaxime sodium. The interaction may be solvent-solvent or solute-solute or solute-solvent type.

Free volume is the average available volume between the molecules of mixture. Free volume is one of the significant factors in explaining the variation in the physico-chemical properties of liquid and liquid mixture. The free space and its dependant properties have close connection with molecular structure and it may show interesting features about interaction, which may occur when two or more liquids are mixed together. This molecular interaction between like and unlike molecules are influenced by structural arrangements along with shape and size of molecules. A liquid may be treated as if it were composed of individual molecules each moving in a volume V_f in an average potential due to its neighbors, that is, the molecules of liquid are not closely packed and there are some free space between the molecules of movement and the volume of is called free volume. Eyring and Kincaid defined free volume as the effective volume in which particular molecules of liquid can move and obey perfect gas law.

From table 1, 2 and 3, it can be easily seen that the V_f values increase with increase in concentration and frequency and same increases up to 308K temperature further it decreases with increase in temperature. Increase in V_f values with increase in concentration and frequency indicate strength of interaction increases gradually where as decrease in V_f values with increase in temperature shows that strength of interaction decreases. It represent that there is strong interaction between solute and solvent molecules.

4. Conclusion

From the present investigation, it is obvious that there exists a specific molecular interaction in aqueous solution of Cefotaxime sodium arising from the hydrogen bond formation between Cefotaxime sodium and water molecule. The strengthening of molecular interaction with increasing concentration, temperature and frequency, is indicated by increase in values of ultrasonic velocity, relative association, specific acoustic impedance and free volume.

References

[1] Roumana, C., Velraj Roumaisa G., Mohammed Kamil M. G., (2008,) Acoustical investigation of molecular

interaction in aqueous antibiotic solution , *J. Pure Appl. Ultrason*., 30, 2008, 97-102.

[2] Roumana, C., Velraj,, G., Akilandeswari, P. E. and Mohammed Kamil M. G., (2009), Acoustical investigation of molecular investigations and staking of aqueous antibiotic Doxycyclin Hyclate, *Proceedings of Eighteenth National Symposium on Ultrasonics, NSU-XVIII, Vellore*, 144-148.

[3] Paliwal,, S. K. and Tabhane,, V. A,(2004), Ultrasonic study of molecular interactions in some aqueous antimicrobials, *J. Pure Appl. Ultrason.*, 26, 105-110.

[4] Swamy, K. M., Ranganathan S., Narayana, K. L. and Bapuji, ,(2009), Synergetic enhancement of antibiotic activity by Ultrasound, *Proceedings of Eighteenth National Symposium on Ultrasonics*, NSU-XVIII, 2009, Vellore, 110-112

[5] Aswale, S. S., Dhote, A. B., Hajare, R. S., Raghuwanshi, P. B. and Aswale, S. R., (2009), Use of ultrasonic velocity to study solute-solvent interaction of Coumaran-3-ones in polar and non-polar solvents**,** *Proceedings of Eighteenth National Symposium on Ultrasonics*, 2009,NSU-XVIII, Vellore, 132-118.

[6] Aswale, S. R., Aswale,, S. S., Dhote, A. B. and Tayade, D. T., ,(2011), Ultrasonic investigation of molecular interaction in Paracetamol solution at different concentration, *J. Chem. Pharm. Res*., 6, 233-236.

[7] Aswale, S. S., Raghuwanshi, P. B., Tayde, D. T. and Aswale, S. R., 2007), Comparative study of intermolecular interactions by acoustic properties of α-bromoacetophenone and Coumaran-3-ones in ethanol and dioxane solvent, *J. Indian Chem. Soc*., 84, 159-164.

[8] Aswale, S. S., Aswale, S. R., Tayade, D. T. and Raghuwanshi, P. B., (2008), Intermolecular free length and Apparent molar volume of Bioactive α-bromoacetophenone and Coumaran-3-ones in ethanol and dioxane solvent**,** *Proceeding of 1st International Society Bio-Technology conference, Gangtok*, 325-330.

[9] Aswale, S. S., Aswale, S. R, Tayade, S. R, and Raghuwanshi, P. B**.**, (2008), Apperent molar compressibility Specific acoustic impedance of α-bromoacetophenone and Coumaran-3-ones in ethanol and dioxane solvent, *J. pure appl. Ultrason*. 30, 62-68.

[10] Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2012) Ultrasonic investigation as tool for study of molecular interaction of Ceftriaxone Sodium at different temperature**,** Sci. *Revs. Chem.commn*. 2(3), 514-518.

[11] Aswale,, S. S., Hajare, R. S. and Aswale, S. R., (2012) Ultrasonic study of Cefotaxime Sodium at different temperature, *National Conference on Recent Researchers in Chemistry, A Journey Towards Social Upliftment*, Wani, 24-25.

[12] Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2012)Relative association, Specific Relaxation time and Free volume of antibiotic Ampicillin Sodium, J. Chem. Pharm. Res., 4(8), 3783-3791.

[13] Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2012) Molecular interaction studies in aqueous antibiotic solution at different temperatures using ultrasonic techniques, J. Pure Appl. Ultrason., 34, 90-92,

[14] Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2012) Ultrasonic investigation as tool for study of molecular interaction of Ceftriaxone Sodium at different temperature, J. Chem. Pharm. Res., 4(5), 2671-2677.

[15] Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2013). Adiabatic compressibility, intermolecular free length, and acoustic relaxation time of antibiotic Ampicillin Sodium, *International Journal of Pharmacy and Pharmaceutical Sciences*, 5(1), 76-79.

[16] Dhote, A. B., Hajare, R. S., Aswale, S. S. and Aswale, S. R., (2015) Acoustic study of aqueous solution of 0.001 Paracetamol at different temperature, *Sunrise Multidisciplinary Reasearch Journal*, Special Issue, 1-4.

[17] Hajare, R. S., Dhote, A. B., Aswale, S. S. and Aswale, S. R., (2015) Study of molecular interaction Of antibiotic drug Ampicillin Sodium at different temperatures by Ultrasonic

Interferometry, *Sunrise Multidisciplinary Reasearch Journal*, Special Issue, 5-6.

[18] Dhote, A. B., Aswale, S. R., Aswale, S. S. and Hajare, R. S., (2016) Ultrasonic studies of molecular interactions in solution of Anti-pyretic drug at 6MHz and 303.15K, *Gurukul International Multidisciplinary Research Journal*, 103-105.

[19] Hajare, R. S., Aswale, S. R., Aswale, S. S. and. Dhote, A. B., (2016) Molecular interaction of aqueous solution of Ceftriaxone Sodium and Ampicillin Sodium by Ultrasonic Interferometry-comparative study**,** *Gurukul International Multidisciplinary Research Journal*, 115-119.

[20] Hajare, R. S., Dhote, A. B., (2017) Study of acoustic and thermodynamic property of aqueous solution of Ceftriaxone sodium and Ampicillin sodium by ultrasonic interferometry- A comparative study, *Bionano Frontier*, 345-347,

[21] Hajare, R. S., Aswale, S. R., Aswale, S. S., (2018) Relative association, Specific Relaxation time and Free volume of antibiotic Ceftriaxone Sodium, *Aaushi International Interdisciplinary Journal*, 25, 47-51

[22] Eyring H., and Kincaid J. F., (1977), *j. Phys*., 6, 728-730.

[23] Baluja, S., (2004), *J. Indian Chem. Soc*., 81, 570-572.