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Research Article

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Relative association, specific relaxation time and free volume of antibiotic ampicillin sodium

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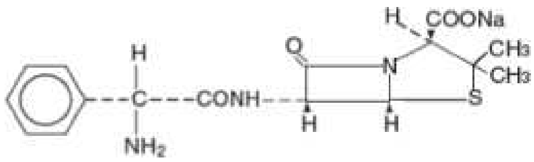
ABSTRACT

There are many techniques available to study physical properties to interpret the molecular interaction in liquids, liquid mixtures and solutions. The study of ultrasonic waves through solution is found to be quite interesting. The study of ultrasonic waves through solution is used for knowing the nature and strength of intermolecular forces and their interaction in liquids, liquid mixtures and solutions. Thermo-acoustical and its allied properties are very helpful in predicting the physico-chemical behavior and molecular interactions occurring in liquids, liquid mixtures and solutions. Hence this motivates the researchers to take up the research project in the field. Ultrasonic velocity, density and viscosity have been measured for antibiotic ampicillin sodium in water at different concentrations, temperatures and different frequencies such as 2MHz, 4MHz and 6MHz, with a view to investigate the exact nature of molecular interactions. From the experimental data, ultrasonic parameters such as relative association, specific acoustic relaxation time and free volume have been computed. The results have further been used to interpret the nature and strength of molecular interactions in the aqueous solution of ampicillin sodium.

Key words: Ultrasonic velocity, hydrogen bonding, molecular interactions, antibiotic ampicillin sodium.

INTRODUCTION

Ultrasonic non-destructive testing is resourceful technique that can be appropriate to study molecular interactions in liquids, liquid mixtures and solutions. Ultrasonic propagation parameters yield valuable information regarding the behavior of solutions, because intermolecular association, complex formation, dipole interaction and related structural changes affect the compressibility of the system which produces corresponding variations in the ultrasonic velocity. Ultrasonic technique has been adequately employed to investigate the properties of any substance to understand the nature of molecular interactions in pure liquid,[1] liquid mixtures[2-3] and solutions[4]. Drug action, although complex result from various kinds of physico-chemical interactions, eg. Ion-dipole, ionic or covalent, hydrogen bonding, charge transfer interactions, hydrophilic interactions etc.[5-6] All the formokinetic processes involve transport of drug across biological membranes, which can be understood by transport property measurements such as ultrasonic velocity, viscosity, thermal conductivity and diffusion. A number of researchers [7-12] have investigated the molecular interaction in aqueous solution of different antibiotics in the recent years. Ampicillin sodium is beta-lactum antibiotic derived from penicillin nucleus, 6-aminopenicillanic acid, that has extensively been used to treat bacterial infections in pharmaceuticals. It is used to treat urinary tract infections, otitis media, pneumonia, haemophilus influenza, and salmonellosis and listeria meningitis.



(Ampicillin sodium)

Literature survey reveals that no work has been reported on ultrasonic interferometric study of aqueous ampicillin sodium to investigate the exact nature of molecular interactions. In continuation of our work,[13-19] in the present paper, experimental studies were carried out to investigate solute-solvent interaction of aqueous solution of ampicillin through ultrasonic velocity measurements at different temperatures, concentrations and frequencies. The main purpose of investigation is to study molecular interaction, drug absorption, transmission activity of aqueous solution of ampicillin sodium.

EXPERIMENTAL SECTION

Antibiotic drug ampicillin sodium obtained from Aristo Pharmaceuticals Private Limited was used. The chemicals used were of analytical grade. Double distilled water was used for preparation of solutions. A special thermostatic water bath arrangement was made for density, ultrasonic velocity and viscosity measurements and temperature variation was maintained within $\pm 0.01^0$C Multi frequency interferometer (Mittal Enterprises, Model F-83) with accuracy of ±0.03% and frequency 2 MHz, 4MHz, 6MHz was used in the present work for measurement of ultrasonic velocities of solutions. Densities of solutions were measured using specific gravity bottle. These values were accurate up to ± 0.1 kg/m^3. All the weighing was made on CA-124 (CB/CA/CT series, Contech) digital electronic balance having an accuracy of ± 0.0001g. Viscosities of the solution were measured by Ostwald's viscometer.

RESULTS AND DISCUSSION

In the present investigation, measurements of densities, viscosities and ultrasonic velocities of solvent water and an antibiotic ampicillin sodium solution in water have been made.

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

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

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

Relaxation time is evaluated by equation

$$\boldsymbol{\tau = 4/3\beta.\eta} \quad \ldots\ldots\ldots (2)$$

Where, β=adiabatic compressibility **η** =viscosity of experimental liquid.

Free volume is calculated by following equation

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

Where, M_{eff} is effective molecular weight, K is a temperature independent constant which is equal to 4.28 x 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.

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

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Relative association (R_A)	Specific relaxation time $\tau x10^{-10}$ (sec)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1456.63	1024.94	0.8514	1.0390	5.2203	1.1920
	0.01	1528.85	1028.97	0.8896	1.0264	4.9321	1.3770
	0.1	1598.42	1033.77	0.9639	1.0160	4.8660	1.7567
308.15	0.001	1526.69	1019.55	0.7252	1.0278	4.0695	1.0100
	0.01	1526.79	1022.23	0.7517	1.0304	4.2061	1.0700
	0.1	1598.55	1027.55	0.8049	1.0201	4.0872	1.3400
313.15	0.001	1492.82	1017.30	0.6651	1.0340	3.9122	0.8540
	0.01	1563.28	1018.65	0.6821	1.0196	3.6534	0.9560
	0.1	1601.06	1025.79	0.7353	1.0186	3.7289	1.1700

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

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Relative association (R_A)	Specific relaxation time $\tau x10^{-10}$ (sec)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1456.63	1024.94	0.8514	1.0316	4.3362	1.3699
	0.01	1528.85	1028.97	0.8896	1.0356	4.5127	1.4719
	0.1	1598.42	1033.77	0.9639	1.0394	4.8387	1.7642
308.15	0.001	1526.69	1019.55	0.7252	1.0316	3.7102	1.0800
	0.01	1526.79	1022.23	0.7517	1.0351	3.8544	1.1400
	0.1	1598.55	1027.55	0.8049	1.0392	4.0741	1.3400
313.15	0.001	1492.82	1017.30	0.6651	1.0429	3.4075	0.9470
	0.01	1563.28	1018.65	0.6821	1.0444	3.4879	0.9900
	0.1	1601.06	1025.79	0.7353	1.0513	3.7260	1.1700

Table 3: Acoustic parameters of aqueous solution of Ampicillin sodium at 6MHz.

Temperature (K)	Concentration (M)	Ultrasonic Velocity (m/s)	Density (Kg/m^3)	Viscosity $\eta x10^3$ (NSm^{-2})	Relative association (R_A)	Specific relaxation time $\tau x10^{-10}$ (sec)	Free Volume $V_f x10^{-8}$ (m3/mole)
303.15	0.001	1456.63	1024.94	0.8514	1.0314	4.1468	1.4166
	0.01	1528.85	1028.97	0.8896	1.0354	4.3140	1.5224
	0.1	1598.42	1033.77	0.9639	1.0393	4.6272	1.8243
308.15	0.001	1526.69	1019.55	0.7252	1.0483	3.5448	1.1200
	0.01	1526.79	1022.23	0.7517	1.0512	3.6676	1.1800
	0.1	1598.55	1027.55	0.8049	1.0563	3.8966	1.3900
313.15	0.001	1492.82	1017.30	0.6651	1.0464	3.2553	0.9800
	0.01	1563.28	1018.65	0.6821	1.0500	3.3357	1.0200
	0.1	1601.06	1025.79	0.7353	1.0567	3.5572	1.2200

Measured values of density, viscosity, ultrasonic velocity and calculated relative association, acoustic relaxation time and free volume of aqueous ampicillin sodium solution at different concentrations, temperatures and at different frequencies such as 2MHz, 4MHz and 6MHz are given in Table 1, 2 and 3. Respective graph of ultrasonic velocity, relative association, acoustic relaxation time and free volume as a function of concentration, temperature and frequency are presented in figures 1, 2, 3and 4.

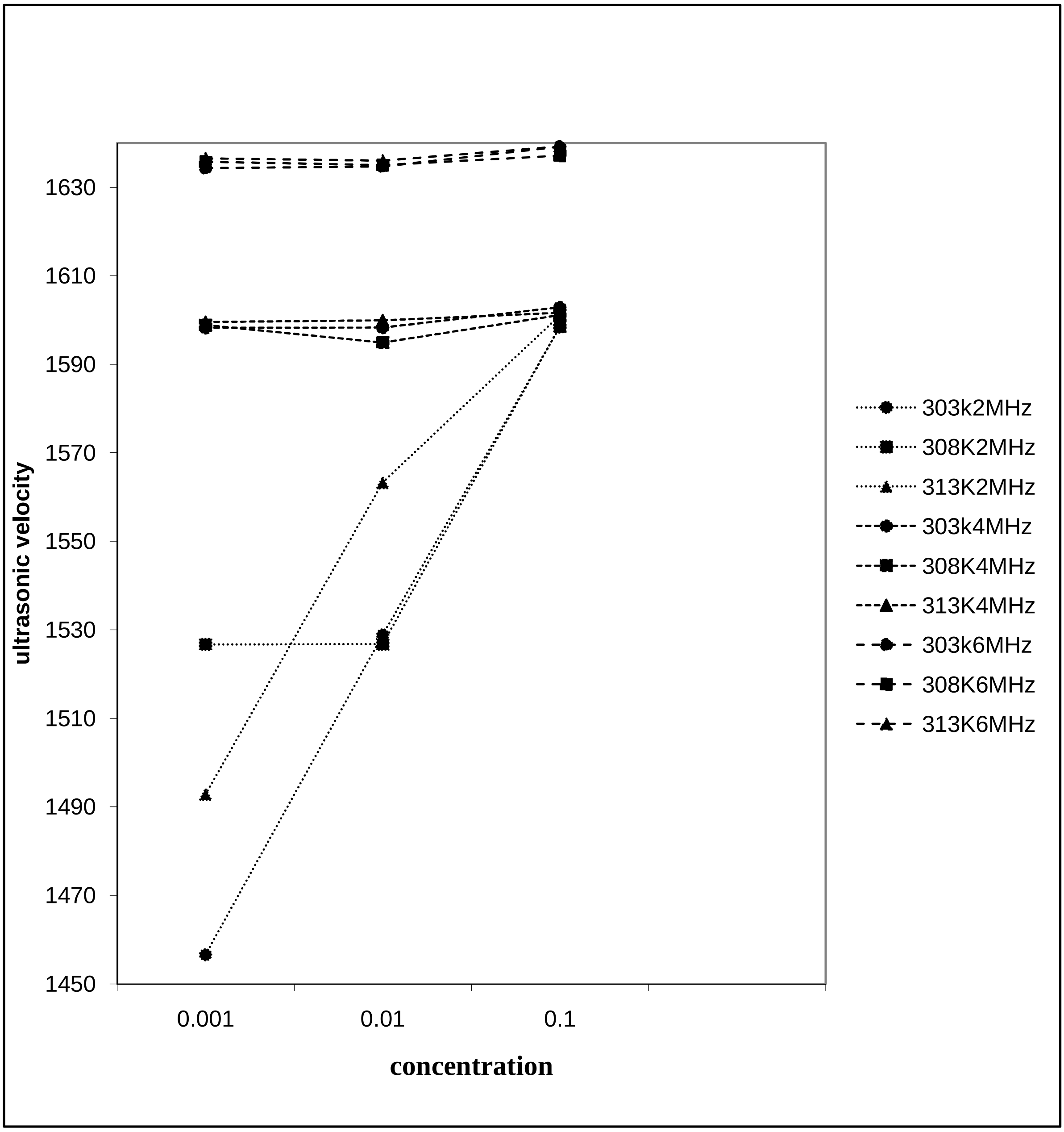


Fig. 1 variation of ultrasonic velocity with concentration, temperature and frequencies.

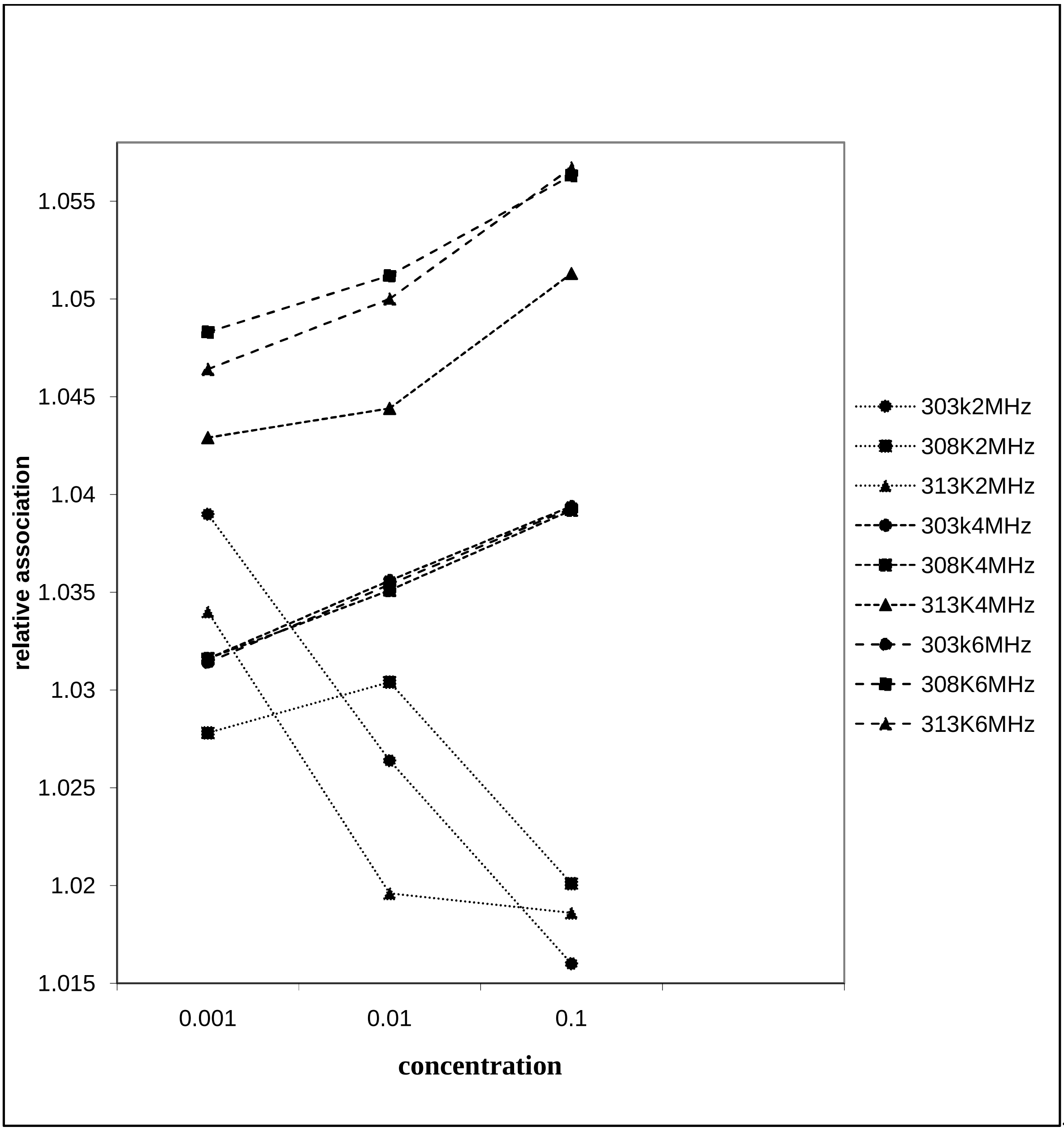


Fig. 2 variation of relative association with concentration, temperature and frequencies

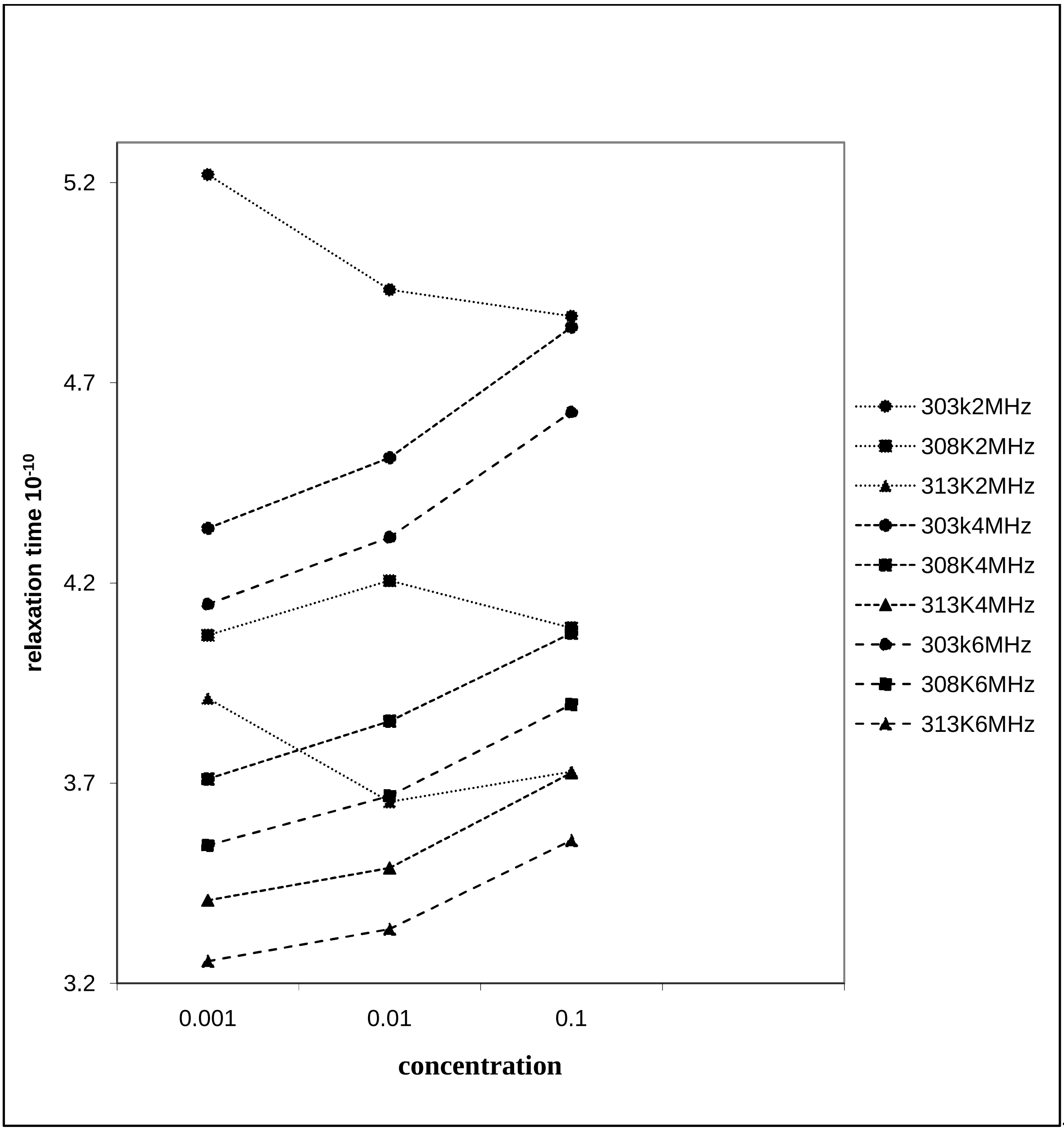


Fig. 3 variation of relaxation time with concentration, temperature and frequencies

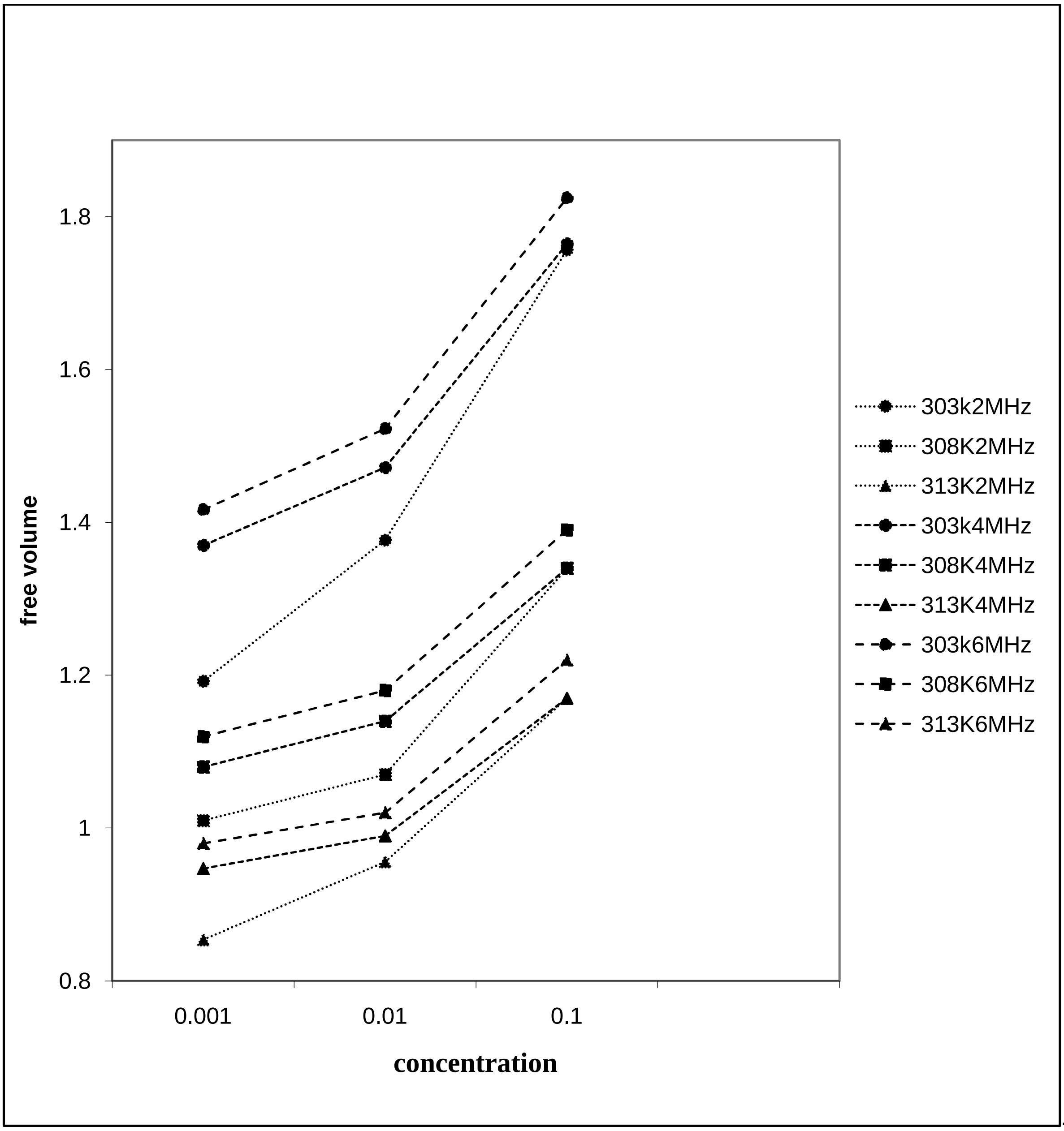


Fig. 4 variation of free volume with concentration, temperature and frequencies

To explore the nature and type of existing interactions some thermo-acoustical parameters have been determine and their extremities and trends analyesed in the light of existing structural changes.

The perusal of the Tables 1, 2 and 3, clearly reveals that measured parameters density and viscosity of aqueous solution of ampicillin sodium increases with increase in concentration and the same deceases with increase of temperature. As concentration of ampicillin sodium increases, number of particles in a given region increases lead into shrinkage of a volume of solution, thereby increasing density. Further, the increase in number of particles simply increases the frictional resistance between the layers of medium resulting in increase of velocity. The decreasing values of density and viscosity with temperature are due to decrease of molecular forces which in turn may be due to increasing the thermal energy of the system. Ultrasonic velocity values of aqueous solution of ampicillin sodium increases with increase in concentration and frequency. And same is non-linear with increase of temperature as shown in Fig.1. As concentration increases number of molecules in the medium increases, making the medium to be denser, which leads to lesser compressibility resulting in quick transfer of sound velocity and hence ultrasonic velocity increases with increase of concentration and frequency? The same trend is observed by Arul et al.[20] The increased values of ultrasonic velocity indicate maximum molecular association among the molecules of aqueous ampicillin sodium solution. At 4MHz at 308K and at 6MHz at 308K and 313K ultrasonic velocity slightly decreases up to 0.01M and then increases. This may due to self-association of solvent molecule and very weak dipole-induced dipole interaction between components of molecules. The increasing values of density, viscosity and ultrasonic velocity indicate that there is strong solute-solvent interaction in aqueous solution of ampicillin sodium.

Relative association is the measure of extent of association of components in the medium. It is a property of understanding the molecular interaction in liquid mixtures and solutions. The relative association depends on either of breaking up of the solvent molecules on addition of solute to it or the salvation of ions that are present. The former results in decrease of R_A and latter in increase of R_A. Referring to fig. 2 and Table 1, 2 and 3, it is observed that at 2MHz, R_A decreases with increase of concentration and temperature where as at 4MHz and 6MHz it increases with increase of concentration and temperature. At 2MHz, R_A decreases which is due to the breaking up of the solvent molecules on addition of solute where as at 4MHz and 6MHz, R_A increases, which is due to salvation of ions. These variations in R_A suggest the specific molecular interactions among the components. The interaction may be solute-solute, solvent-solvent, solute-solvent type due to formation of hydrogen bond.

Specific relaxation time is the time taken for the excitation energy to appear as translational energy. It depends on temperature and on impurities. From fig. 3 and Table 1, 2 and 3, it is observed that the values of relaxation time decreases with increase in temperature and frequency and increases with increase of concentration except at 2MHz, it shows variations. The variations in specific relaxation time are mainly due to the change in viscosity of solutions due to both concentration and temperature. The relaxation time is the order of 10^{-12}sec is due to the structural relaxation process [21] and such situation suggests that the molecules get rearranged due to co-operative process.[22] This indicates the presence of specific molecular interaction among ampicillin sodium and water.

Free volume is one of the important factors in explaining the variations in physico-chemical properties of liquids, liquid mixture and solutions. It is defined as average available volume between molecules of mixture. It is evident from fig. 4 and Table 1, 2 and 3 that free volume increases with increase in concentration and frequency and same decreases with increase in temperature. With the increase of free volume with concentration and frequency the free space between ampicillin sodium and water molecules increases, which denotes that the association of solute decreases with water. Hence molecular binding between solute and water molecules gets loosened as concentration increases or the solution is of structure breaking in nature. This decreases the strength of interaction with increase of concentration and frequency where as opposite trend of free volume with increase of temperature, increases close packing of molecules. This strengthening the molecular interaction with increase of temperature.

CONCLUSION

From the preservative taken for study, it is concluded that there is a specific molecular interaction, which may be solute-solute, solvent-solvent solute-solvent type due to formation of hydrogen bond.

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REFERENCES

[1] MG Sheshagiri Rao. *Indian J. Pure Appl. Phys*., **1971**, 9, 169-172.
[2] MV Kaulgud; KJ Patil. *Indian J. Pure Appl. Phys*., **1975**, 13, 238-242.
[3] Pankaj; C Sharma. *Ultrasonics*, **199**, 29, 344-347.
[4] VS Soitkar; SN Jajoo. *Acoust. Lett*., **1984**, 79(2), 1991-1996.
[5] A Karol Kovas. Essentials of Medicinal Chemistry, 2^{nd} Ed. Wiley, New York, **1988**, chap. 3.
[6] JB Stenleke. Founations of molecular Pharmacology, Athlone Press, London, **1975**.

[7] PS Ramesh; C Indumati; D Teethe; C Rakkappan. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 113-118.
[8] A Panneerselvan; D Geetha. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 418-425.
[9] C Roumana; G. Velraj. Roumaisa, M. G. Mohammed Kamil, *J. Pure Appl. Ultrason*., **2008**, 30, 97-102.
[10] C Roumana; G Velraj; PE Akilandeswari; MG Mohammed Kamil. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 144-148.
[11] KM Swamy; S Ranganathan; KL Narayana; Bapuji. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 110-112.
[12] S Shriprasad; PE Akilanadeshwari; PA Abdul Mehaboob; GS Gayatri; MG Mohammed Kamil. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 149-153.
[13] SS Aswale; AB Dhote; RS Hajare; PB Raghuwanshi; SR Aswale. *Proceedings of Eighteenth National Symposium on Ultrasonics*, *Vellore*, **2009**, 132-138.
[14] SR Awake; SS Aswale; AB Dhote; DT Tayade. *J. Chem. Pharm. Res*., (6), **2011**, 233-236.
[15] SS Aswale; PB Raghuwanshi; DT Tayde; S.R. Aswale. *J. Indian Chem. Soc*., **2007**, 84, 159-164.
[16] SS Aswale; SR Aswale; DT Tayade; P. B. Raghuwanshi. *Proceeding of 1st International Society Bio-Technology conference*, *Gangtok*, **2008**, 325-330.
[17] SS Aswale; SR Aswale; DT Tayade; PB Raghuwanshi. *J. pure appl. Ultrason*, **2008**, 30, 62-68.
[18] SS Aswale; SR Aswale; RS Hajare. *J. Chem. Pharm. Res*., **2012**, 4(5), 2671-2677.
[19] SR Aswale; SS Aswale; RS Hajare. *Sci. Revs. Chem. commn*. **2012**, 2(3), 514-518.
[20] J Arul; L Palaniappan. *Indian J. Pure Appl. Phys*., **2001**, 39, 561-564.
[21] LE Kinser; AR Frey. Fundamentals of acoustics. Wiley Eastern New Delhi, **1989**.
[22] A Ali; S Hyder; AK Nain. *J. phys*., **2000**, 74B, 63-67.