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STUDY OF MOLECULAR INTERACTIONS OF CHLORPROMAZINE DRUG AT DIFFERENT TEMPERATURES BY ULTRASONIC AND VISCOMETRIC MEASUREMENTS

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Abstract

Chlorpromazine drug is a drug used for antipsychotic, neuroleptic, psychosedative.

Molecular interactions of Chlorpromazine hydrochloride with dioxane - water have been investigated using experimental techniques. The density, viscosity and ultrasonic velocity of the mixture solutions have been experimentally measured using standard techniques. From these values various parameters, such as Adiabatic Compressibility, Free Volume, Rao's constant, Relative Association, have been derived which show qualitatively the strength of intermolecular interactions between solute and solvent. Such studies have been done at various temperatures ranging from 298 K to 313 K. It has been found that at all temperatures and low concentrations; there is a strong interaction between the solute and the solvent. It is due to H-bonding between solvent and solute molecules.

KEYWORDS*: Chlorpromazine hydrochloride, Ultrasonic Studies, Inter Molecular interactions.*

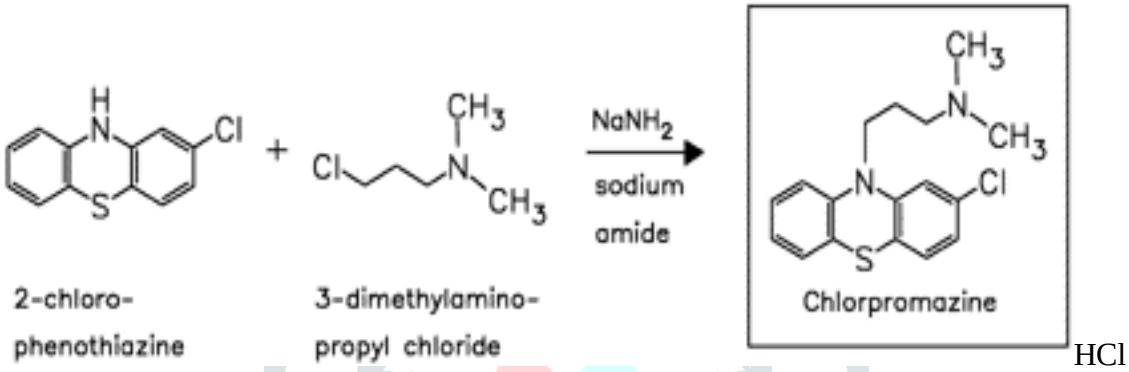
Introduction

Ultrasonic waves, in recent years, have acquired the status of and important probe for the structure and properties of matter in basic science. Ultrasonic techniques are best suited for physicochemical studies of systems. The unique feature of sound wave property is that it gives direct and precise information of the adiabatic properties of solution. Most of the information extracted from ultrasonic study of fluids is confined to the determination of hydration number and compressibility[1-3]. Determinations of ultrasonic velocity and absorption coefficient have furnished method for studying molecular and structural properties of liquids. As there exists intimate relationship between the ultrasonic velocity and chemical or structural characteristics of molecules of liquids, this gives a property of basic importance to ultrasonic velocity in molecular theory of liquids[11].

Viscometry [4-5] is an important tool in order to elucidate the solute – solvent interaction and nature of a solute as a structure maker or a structure breaker. Viscosity provides an insight into the stage of association of the solute and extent of its interaction with solvent. The nature and degree of molecular interaction in different solution depends upon several factors i.e. the nature of the solvent, the structure of the solute and also the extent of solvation taking place in the solution. The viscosity of liquid depends on its molecular size and shape, the intermolecular attraction, and the liquid structure. Those liquids flow slowly are said to have high viscosity and those which flow readily are said to have low viscosity. The viscous drag can be overcome and a constant velocity gradient between layers can be maintained if an external force is applied in the direction of motion.

Viscosity and its parameters provide valuable information regarding the shapes and size of molecules[6]. Grouping of solvents into classes often is based on the nature of the intermolecular forces because the manner where by solute and solvent molecules are associated with one another brings about a marked effect on the resulting properties. The measurement of viscosities of electrolyte in solution provides an excellent method of obtaining data on solute solvent and solute- solute interaction. Medicinal industry seeks understanding of a drug's physico-chemical behavior and intermolecular interaction with a solvent. The drug-solvent molecular interaction and its temperature dependence play an important role in the understanding of drug action[7-8]. Acoustical and Viscometric properties provide valuable clues for solute- solvent interactions in the solution mixture, which is helpful in predicting the absorption of drug and transport of drug.

Chlorpromazine drug which is chemically designated as *[3-(2-Chloro-10-H-phenothiazin-10-yl)-N,N-dimethyl-propan-1-amine]*. The drug used for antipsychotic, neuroleptic, psychosedative. Its chemical formula is $C_{17}H_{19}ClN_2S$ and is often formulated as the hydrochloride salt. Its formula is $C_{17}H_{19}ClN_2S \cdot HCl$ representing a molecular weight of 355.33 g/mole. For understandingof Chlorpromazine interaction with the dioxane water its molecular structure has been shown in Fig.



Experimental

Solvent dioxane used in the present work was of AR grade and were purified and dried by the usual procedure. Densities, viscosities and ultrasonic velocities were measured at 298K to313 K over a wide range of composition. Densities were determined by using bicapillary pyknometer. The viscosities were measured by precalibrated Ostwald type viscometer. Ultrasonic velocity measurements were made by using an ultrasonic interferometer (Mittal Enterprises, New Delhi) at a frequency of 2MHz with a tolerance of ± 0.005%. All the measurements were carried out at 298K to 313 K The drug Chlorpromazine hydrochloride has been used in this study. All the mixtures were prepared in double distilled water on a morality basis by using Digital Balance with an accuracy of ± 0.001g. The concentration of the drug- dioxane water mixture has been varied in the range 0.02 M to 0.1 M. Standard experimental techniques[9-11] have been used for measurement of density, viscosity and ultrasonic velocity in the mixture solution at different temperatures.

Acoustic parameters such as apparent molar compressibility (ϕ_k), apparent molar volume (ϕ_v), adiabatic compressibility (β_s), specific acoustic impendence (Z), intermolecular free length (L_f), Limiting apparent molar volume (ϕ^0_v), Limiting apparent molar compressibility (ϕ^0_k) were determined using following relations.

Ultrasonic velocity	$u = \lambda\upsilon$ ----------	1
Adiabatic compressibility	$\beta_s = 1/ u^2_s \rho_s$ ----------	2
Apparent molar volume	$\phi_v = 10^3(\rho_0-\rho_s)/m-\rho_0 \rho_s + M/\rho_0$ ----------	3
Apparent molar compressibility	$\phi_k = 10^3(\rho_0\beta_s-\rho_s\beta_0)/m-\rho_s \rho_0 + \beta_s M/\rho_s$ ----	4
Intermolecular free length	$L_f = K (\beta_s)^{1/2}$ ----------	5
Specific acoustic impendence	$Z = \rho.u$ ----------	6
Limiting apparent molar volume	$\phi_v = \phi^0_v + S_v C^{1/2}$ ----------	7
Limiting apparent molar compressibility	$\phi_k = \phi^0_k + S_k^{1/2}$----------	8

In the present paper, we present the results obtained for experimental study for understanding the intermolecular interactions of the Chlorpromazine hydrochloride drug with dioxane- water for different concentrations and at different temperatures. We limited our study to the temperature range of 298K to 313 K. Experimental methods used for measuring density (ρ), viscosity (η) and ultrasonic velocity (U) of the mixture solution have been presented in the next sections. Using these measured values, some quantities such as

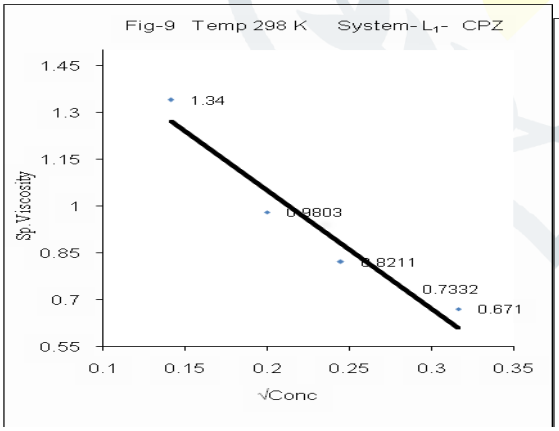
adiabatic compressibility, free volume, intermolecular free length, Rao's constant, relative association, etc., have been derived.

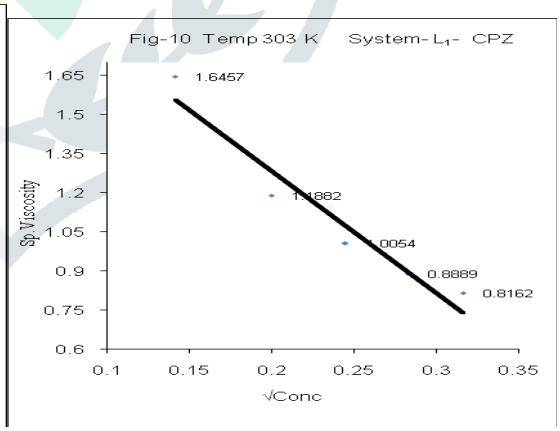
Table-1

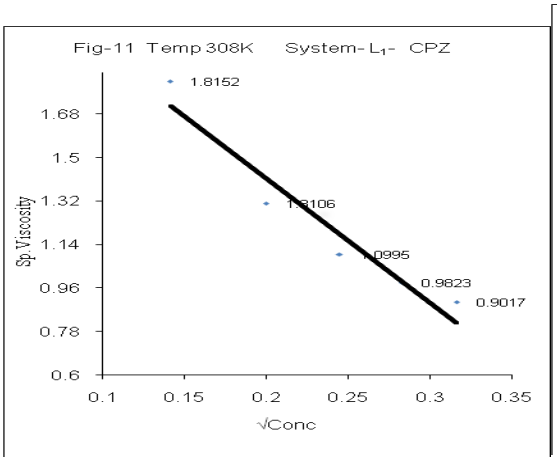
Viscosities, Relative Viscosity, Sp. Viscosity, Densities at different temperatures System-CPZ in 20% Dioxane-Water medium

Conc mol dm^{-1}	At 298K					At 303K				
	Density $x10^3$ Kg m^{-3}	Time flow in sec	Viscosity $x10^{-3}$ Nsm^{-2}	Relative Viscosity	Sp Viscosity	Density $x10^3$ Kg m^{-3}	Time flow in sec	Viscosity $x10^{-3}$ Nsm^{-2}	Relative Viscosity	Sp Viscosity
0.02	1.03304	78.1	1.19896	1.16545	1.34042	1.03209	76.8	1.17061	1.20969	1.64575
0.04	1.03323	78.5	1.20533	1.17182	0.98037	1.03216	77.1	1.17526	1.21450	1.18822
0.06	1.03359	78.8	1.21035	1.17679	0.82116	1.03266	77.6	1.18346	1.22297	1.00541
0.08	1.03402	79.2	1.21700	1.18291	0.73324	1.03294	77.9	1.18835	1.22803	0.88894
0.1	1.03415	79.6	1.22330	1.18761	0.67100	1.03315	78.3	1.19470	1.23458	0.81622
	At 308 K					At 313 K				
0.02	1.03009	75.6	1.15906	1.23265	1.81521	1.02911	73.4	112026	1.25753	1.99955
0.04	1.03045	75.9	1.16407	1.23797	1.31069	1.02932	73.9	1.12812	1.26636	1.45890
0.06	1.03089	76.3	1.17070	1.24503	1.09954	1.02986	74.2	1.13329	1.27217	1.21538
0.08	1.03105	76.8	1.17855	1.25338	0.98234	1.03006	74.6	1.13963	1.27927	1.07818
0.1	1.03158	77.2	1.18530	1.26056	0.90176	1.03041	75.2	1.14198	1.29000	0.99895

System-CPZ in 20% Dioxane-Water medium at different temperatures







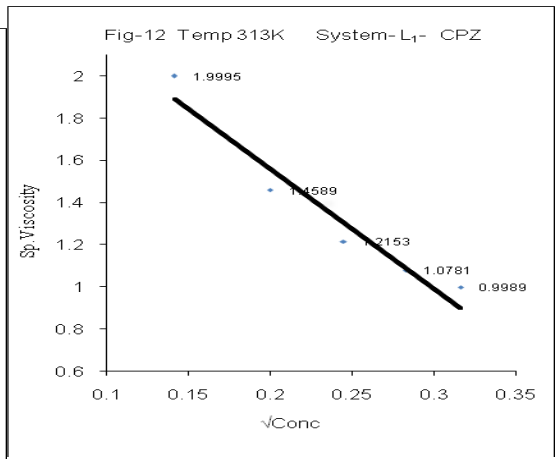


Table- 2

Density, Ultrasonic Velocity and related thermodynamic Parameters at different temp.

System-CPZ 20% Dioxane-Water medium

Temp T (K)	Conc. mol. dm^{-3}	Density ρs Kgm^{-3}	Ultrasonic Velocity(u) m/s	$\beta_{s\ x10^{-10}}$ Pa^{-1}	Φv $x10^{-5}$ m^3mol^{-1}	Φk $x10^{-14}$ m^3mol^{-1} Pa^{-1}	$L_{f\ x}10^{-11}$ (m)	Z x 10^5 Kg m^{-2} sec^{-1}	Relative association R_A $X10^{-3}$
298K	0.02	1033.04	1575.4	3.7382	-41.2	-150.479	3.9869	16.6236	1006.26
	0.04	1033.23	1578.6	3.7356	-3.84	-69.6034	3.9856	16.6308	1006.37
	0.06	1033.59	1581.1	3.7320	8.33	-42.9305	3.9836	16.6418	1006.61
	0.08	1034.02	1584.6	3.7272	14.3	-29.7793	3.9811	16.6559	1006.89
	0.1	1034.15	1589.8	3.7249	18.2	-21.5409	3.9798	16.6622	1006.93
303K	0.02	1032.09	1579.5	3.9039	-52.0	-72.8134	3.9516	16.2595	1016.26
	0.04	1032.16	1583.0	3.8878	-8.39	-33.7004	4.1000	16.2936	1015.64
	0.06	1032.66	1586.2	3.8736	4.72	-20.6503	4.0926	16.3273	1015.6
	0.08	1032.94	1590.1	3.8555	11.8	-14.5436	4.0830	16.3679	1015.12
	0.1	1033.15	1594.1	3.8295	16.1	-11.6627	4.0692	16.4250	1014.22
308K	0.02	1030.09	1588.7	3.8462	-45.3	-91.536	4.1116	16.3650	1012.70
	0.04	1030.45	1591.3	3.8323	-6.24	-42.8846	4.1042	16.3975	1012.50
	0.06	1030.89	1598.1	3.7982	6.63	-30.0964	4.0858	16.4746	1011.50
	0.08	1031.05	1600.8	3.7848	13.4	-21.0423	4.0786	16.5050	1011.08
	0.1	1031.58	1601.2	3.7809	17.1	-14.8053	4.0766	16.5176	1011.52
313K	0.02	1029.11	1609.2	3.7524	-46.9	-127.444	4.0931	16.5604	1009.85
	0.04	1029.32	1609.6	3.7498	-6.71	-58.0803	4.0917	16.5679	1009.97
	0.06	1029.86	1610.1	3.7455	6.17	-35.4401	4.0893	16.5817	1010.40
	0.08	1030.06	1610.8	3.7415	13.0	-23.9369	4.0872	16.5922	1010.45
	0.1	1030.41	1611.2	3.7384	17.0	-17.0102	4.0855	16.6019	1010.71

Results and discussion

Table 1 shows viscosities, relative viscosity, sp. viscosity, densities at different temperatures at different concentrations. Viscosity of liquid solutions decreases with decrease in concentration of antipsychotic drugs salts solution in 20% dioxane -water mixture. The increase in viscosity with increase in concentration may be attributed to the increase in solute solvent interactions.

Table 2 shows that density (ρ), ultrasonic velocity (u) increases with increase in concentration for CPZ 20% dioxane-water system. The increase in ultrasonic velocity is due to decrease in intermolecular free length (L_f) as shown in table 2. This suggests that there is a strong interaction between *[3-(2-Chloro-10-H-phenothiazin-10-yl)-N,N-dimethyl-propan-1-amine]* and solvent molecule. Adiabatic compressibility (β_s) is a measure of intermolecular association or repulsion calculated from the measured ultrasonic velocity (u) and density (ρ). Adiabatic compressibility is found to decrease with increase in concentration. Since adiabatic compressibility is inversely related to the product of density and ultrasonic velocity based on this the compressibility is expected to decrease which has observed in the present case. When the sound waves travel through the solution, certain part of it travels through the medium and rest gets reflected by the ion i.e. restriction for flow of sound velocity by the ions. The character that determines the restriction movement of sound waves is known as acoustic impendence (Z). It has been found that acoustic impendence increases with increase in concentration. The apparent molar compressibility (ϕ_k) explains the solute-solvent and solute- solute interactions in solution and was calculated by using the equation no. 4. The apparent molar volume (ϕ_v) is defined as the change in volume of solution for the added one mole of a particular component at constant temperature and pressure. It is thermodynamic property which helps in elucidating solvation behavior of electrolyte in solution. Apparent molar volume was evaluated from the density of solution and solvent.

It is evident from the table 2 that ϕ^0_k values are negative. The negative ϕ^0_k values are suggest solute-solvent interaction whereas positive values are due to solute- solute interaction, is further confirmed by ϕ^0_v values which are positive.

In the present study viscosity of liquid solutions increases with increase in concentration of drugs solution in 20% dioxane-water mixture. The increase in viscosity with increase in concentration may be attributed to the increase in solute solvent interactions.

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