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Physicochemical Properties of Cetrizine HCL Inaqueous Solvent Systems at Different Temperatures

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Abstract: *The study of the volumetric behavior of Cetrizine HClas electrolytes in solution provides information useful to elucidate ion–ion, ion–solvent, and solvent–solvent interactions. Apparent molar volumes (Φv), and excess viscosity forCetrizine HCl in aqueous system have been determined from density (ρ) and viscosity (η) measurements at four different temperatures using the ANTON PAAR densitometer and Mansing Survismeter respectively. Various concentrations ofaqueous solutionsof Cetrizine HCl ranging from 0.02 to 0.1 M were prepared. The apparent molar volumes were calculated from the density data. In addition adiabatic compressibility and acoustic impedance is also determined. The concentration dependence of the apparent and partial molar volumes can be used to study ion–ion interactions, whereas the partial molar volumes at infinite dilution provide information on ion–solvent interactions.*

Keywords*: Cetrizine HCl, density, excess viscosity, acoustic impedance.*

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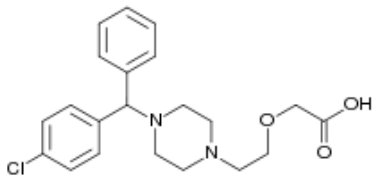
I. Introduction

It is well known that physicochemical characterization of drugs plays a crucial role in all the stages associated to design and development of pharmaceutical dosage forms, especially those intended to parenteral administration[1]. In this context, as a contribution to generation and systematization of physicochemical information about drugs behavior in aqueous system, the main goal of this study was to evaluate the effect of concentration and temperature on the apparent molar volume of drugs in aqueous solvent system at different temperature.The apparent molar volumes ofAntihistamine drug Cetrizine HClin aqueous solvents system and at different temperaturesare reported in the present paper.

Viscosity limits the dissolution rate and there by affect the rapid absorption. E.g. Aqueous Solution of Na-Salicylate showed its rapid appearance in plasma while the same drug in suspension form failed to reach the target as quickly as with aqueous solution.[2]The study of the volumetric behavior of electrolytes in solution provides information useful to elucidate ion–ion, ion–solvent, and solvent–solvent interactions. The concentration dependence of the apparent and partial molar volumes can be used to study ion–ion interactions, whereas the partial molar volumesat infinite dilution provide information on ion– solvent interactions.

DRUG PROFILE-

Structure-



IUPAC name-(±)-[2-[4-[(4-chlorophenyl)phenylmethyl]-1-piperazinyl]ethoxy]acetic acid
Molecular Formula-$C_{21}H_{25}ClN_2O_3$
Molar mass-388.89 g/mol
Cetrizine HCl is a secondgeneration antihistamine used in the treatment of hay fever, allergies, angioedema, and urticaria.It is a major metabolite of hydroxyzine, and a racemicselective H_1 receptorantagonist.Second-generation antihistamines like cetirizine are less able to cross the blood-brain barrier and therefore have diminished effects on the central nervous system compared to first-generation drugs: for instance they are less likely to induce drowsiness or to interfere with memory formation.

EXPERIMENTAL

Materials:

DrugCetrizine HClof high purity was obtained from pharmaceutical industries. Double distilled water was used for the preparation of solutions of different concentration (0.02, 0.04, 0.06, 0.08, 0.1M). The precision of balance used was ± 0.0001g.

Density measurements:

In the present work density of drugCetrizine HCl in aqueous solutions having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, and 0.1M at different temperatures was measured with ANTON PAAR Densitometer at School Of Chemical Sciences, North Maharashtra University, JALGOAN. The ANTON-PAAR densitometer contains two units-

1. Sample holder unit.
2. Reading display unit.

The sample tube starts to oscillate as soon as the instrument is switched on. It is therefore ready to use. The filling of the oscillator with solution is facilitated by the glass syringe. While loading vibrating tube with sample liquid, one has to make sure that the introduction of the liquid must take place slowly, enough to enable the sample liquid to properly wet the walls of the sample tube.To have the more accuracy in the measurement, at each time the density of air was measured before the reading of sample solution. The density of air was found to be in the range of 0.001140 to 0.001148 gm/cm^3. The densities of standard solvent (distilled water) were also measured at different temperatures and are found to be very close to the literature values.Density was measured with an uncertainty of ± 0.000148 g.cm$^{-3.}$

Viscosity measurements:

The solutions of Cetrizine HClhaving concentration of 0.02M, 0.04M, 0.06M, 0.08M, and 0.1M was prepared in aqueous system. The viscosities were measured at 298.15, 303.15, 308.15, 310.15 and 313.15K temperatures for different concentrations. To have more accuracy in the viscosity measurement, the specially designed Mansing Survismeter from Central University Gujrat, Gandhinagar was used to measure the flow time of different solutions. The flow time was measured at the accuracy of ± 0.01 s. The solution viscosities were measured with an uncertainty of ± 2.4×10^{-4} mPa.s by using Mansing Survismeter.The temperature was maintained by circulating water through Mansing Survismeter from an electronically controlled heated bath circulator (MAC-MSW-270). The uncertainty of temperaturewas ± 0.01^{o}C.

Ultrasonic Velocity measurements:

In the present work, the ultrasonic velocity measurements ofCetrizine HCl in aqueous solutions having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, and 0.1M at 303.15K were carried out by an interferometric method. Ultrasonic interferometer,(Mittal Enterprise, New Delhi, Model No.F 81) working at frequency of 3 MHz was used to determine sound velocity. It consists of a high frequency generator and a measuring cell.The calibration of ultrasonic interferometer was done by measuring the velocity in AR grade benzene (C_6H_6) and double distilled water. Experimental values of ultrasonic velocity of benzene at 293, 298, 303 and 313 K were found to be 1316, 1294, 1273, and 1223 ms^{-1} and for distilled water the corresponding values of ultrasonic velocity were found to be, 1499.4, 1511.2, 1520 and 1529.7 ms^{-1} respectively. These values of ultrasonic velocity agree closely with the corresponding standard values. The maximum estimated error has been found to be +0.08 %.

The temperature was maintained by circulating water around the liquid cell from thermostatically controlled adequately stirred water bath (accuracy + 0.1^{o}C) and covering the measuring cell along with its base with a specially made insulated jacket with a window for noting down micrometer readings. The solvent / solution were filled in the measuring cell with quartz crystal and then micrometer was fixed. The micrometer was rotated very slowly so as toobtain a maximum or minimum of anode current (n). A number of maximum reading of anode current were counted. The total distance (d) travel by the micrometer for n=10, was read. The wave length (λ) was determined according to the equation: $\lambda = 2d/n$. The sound velocity (U) of solvent and solutions were calculated from the wavelength and frequency (F) according to equation: $U = \lambda F$.

Data Evaluation:

The apparent molar volumes, (Φv) were obtained from the density results using thefollowing equation -

$$\phi_v = \frac{1000}{c}\left(\frac{d_0 - d}{d_0}\right) + \frac{M}{d_0} \quad \text{.....1}$$

Where M= molar mass of drug, C= concentration in mol.L^{-1} , d= densities of the solutionand d_0= density of the solvent. The apparent molar volumes (ϕv) were plotted against the square root of concentration ($C^{½}$) in accordance with the Masson's equation.[3]

$\Phi v = \Phi v^0 + Sv.C^{½}$ (2)

Where Φv^0 is the limiting apparent molar volume or partial molar volume and Sv is a semi- empirical parameter which depends on the nature of solvent, solute and temperature. The viscosity results for the aqueous solutions of drugs were plotted in accordance with Jones-Dole equation**.**[4]

$\eta_r - 1/C^{1/2} = A + B\ C^{1/2}$(3)

Where $\eta_r = (\eta/\eta o)$ and η, ηo are viscosities of the solution and solvent respectively, C is the molar concentration. The B-coefficients were obtained from the linear plots using the least-square fitting method. The A- coefficient reflects solute -solute interaction [5]and the B-coefficient reflect the solute-solvent interactions. Since in general, A/B <<1, the Jones –Dole equation reduces to,

$\eta r = l + \beta C$, (4)

The relative viscosity data of these solutions have also been fitted in Moulik equation,

$\eta_r^2 = M + K\ C^2$(5)

II. Results And Disussion

The values of the densities (ρ), apparent molar volumes (Φv),Viscosities, Relative Viscosities and Ultrasonic Velocity of drug Cetrizine HClin aqueous solution at different temperatures are shown in table no-1to table no-3.

Table 1: Densities (g.cm^{-3}) and Apparent molar volumes (Φv) of Cetrizine HCl in aqueous solutions of different concentrations and at different temperatures.

Conc. (M)	Densities (g.cm^{-3})				Apparent molar volumes (Φv)			
	298.15	303.15	308.15	313.15	298.15	303.15	308.15	313.15
0.02	0.999392	0.997955	0.996518	0.994447	360.3215	363.1289	366.2578	396.6043
0.04	1.000765	0.999328	0.997891	0.996462	369.8189	372.6789	375.8665	378.6825
0.06	1.002138	1.000701	0.999262	0.99783	377.9847	380.9732	383.4033	386.5719
0.08	1.003512	1.001811	1.000108	0.998407	382.0551	385.2131	387.2641	391.4798
0.1	1.004887	1.003186	1.00206	0.998836	384.4873	388.9256	391.0672	395.9867

Table 2: Viscosities and RelativeViscosities of Cetrizine HClin aqueous solutions of different concentrations and at different temperatures.

Conc. (M)	Viscosities				Relative Viscosities			
	298.15	303.15	308.15	313.15	298.15	303.15	308.15	313.15
0.02	0.940957	0.881324	0.847825	0.817872	1.056068	1.105802	1.179173	1.195721
0.04	0.959657	0.891269	0.863115	0.837248	1.077056	1.118279	1.200438	1.224046
0.06	0.976938	0.909803	0.883662	0.857456	1.096452	1.141534	1.229046	1.253591
0.08	0.994241	0.922536	0.901474	0.879479	1.115871	1.15751	1.253788	1.285787
0.1	1.005918	0.945359	0.921036	0.895531	1.128977	1.186146	1.280996	1.309256

Table 3: Ultrasonic Velocities (m.s^{-1}) of Cetrizine HClin aqueous solutions of different concentrations and at different temperatures.

Concentration (M)	Ultrasonic Velocities (m.sec^{-1})			
	298.15	303.15	308.15	313.15
0.02	1548.3	1556.1	1563.9	1571.7
0.04	1551.3	1559.7	1567.5	1575.3
0.06	1555.6	1563.3	1571.1	1578.9
0.08	1559.1	1566.9	1574.7	1582.5
0.1	1562.7	1569.5	1578.3	1586.1

Table no-1reveals that densities of Cetrizine HClsolutions under investigation decrease with increase in temperature and increases with increase in concentration. Such observations were previously made by Comesana et al.[6], Lee et al.[7],[8] and Nikumbh et al.[9] for other solutions. The values of Φvincreases with increase in concentration. The Φv values of Cetrizine HClunder investigation in aqueous solvent systems are large and positive suggests presence of strong solute-solvent interactionspromotes structure making effect.[10]Table no-2 represents the variation of viscosity (η) of solution as a function of molarity (c) of solution at temperatures of 298.15K, 303.15K, 308.15K and 313.15K.Variation in viscosity indicates the presence of intermolecular interactions between the drug molecules and solvent molecules. Viscosity of solution increases

with the increase in concentration of solution. The increasing concentration of drugs supports non rupturing of drug molecules and hence there is increase in viscosity. Similar increase in viscosity has also been reported by V. Syamala et.al in binary mixtures of dimethyl sulphoxide with chloro and nitro substituted aromatic hydrocarbons at T = 303.15 K. [11].

From table no-3**,** it is seen that the ultrasonic velocity (U) of solutions increases with the increase in molarity (c) of solution for all the systems. As density of solution increases the number of particles in a given region increases and this leads to quick transfer of sound energy and thus velocity also increases. This suggests the disruption of solvent structure with the addition of drug molecules. Similar increase in velocity has been reported by S. Thirumaran et.al in binary liquid mixtures of some aromatic hydrocarbons with dimethylsulphoxide at 303.15 K.[12]

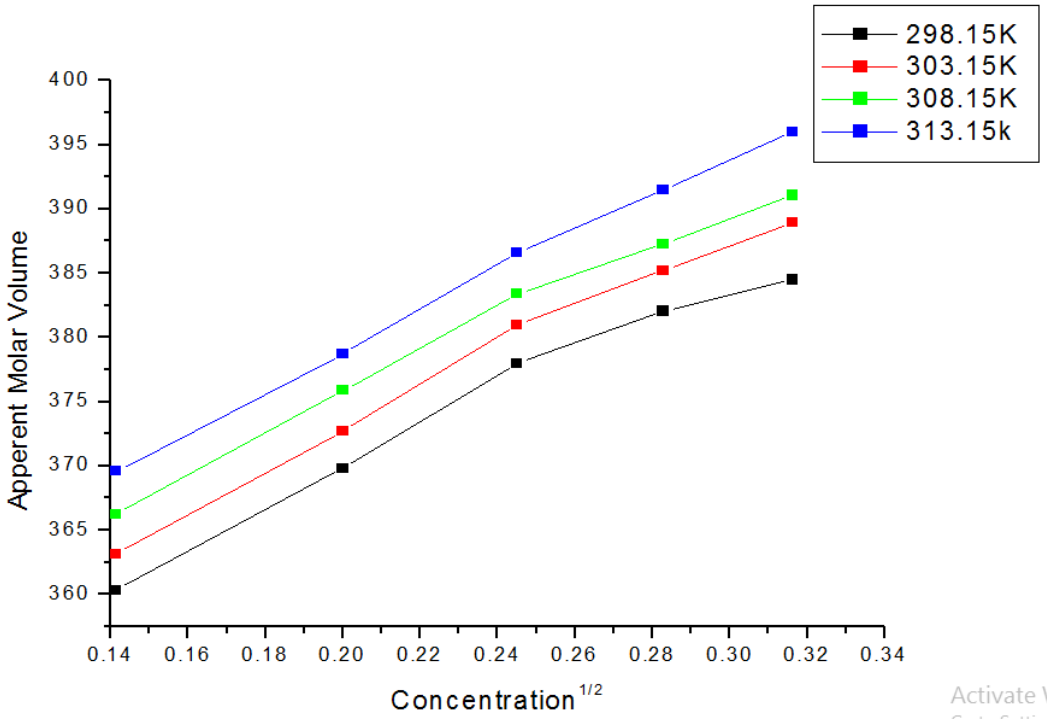


Fig- 1- Plot of Apperent Molar Volume Φv ($cm^3.mol^{-1}$) versus $C^{½}$forCetrizine HCl solutions in aqueous system at different temperature.

Fig. 1 is representative plot which represents variation of Φv with $C^{½}$ in aqueous system. It is observed that plot is linear indicates strong solute- solvent interactions. Φv values also increases linearly with increase in temperature. Mishra, Prasad and Ahluwalia[13], using the model, observed that overlap of co-sphere of two ionic species shows an increase in volume where as overlap of hydrophilic-hydrophobic groups and ion hydrophobic groups show decrease in volume. The positive value of Φv studied in the present investigation suggests that the ion-ion and ion-hydrophilic group interactions are stronger than the ion-hydrophobic interaction that results in an increase in volume.

From the experimental data of density, viscosity and ultrasonic velocity of solutionsvarious acoustical parameters like adiabatic compressibility (βs),Intermolecular free length (Lf), Acoustic Impedance (Z) and Intermolecular free length (Lf)were calculated using following standard equations:

Adiabatic compressibility (βs): $100/ U^2\rho$

Acoustic Impedance (Z): $U\rho$.

Intermolecular free length (Lf): $K\beta^{1/2}$ where K is a Jacobson Constant.

All above thermodynamic parameters for different drugs are given in table no-6 to table no-8.

Table no- 4: Adiabatic compressibility ($\beta a X 10^{-10}$) (m^2N^{-1}) and Acoustic Impedance ($Z X 10^6$) (Nm^{-2}) of Drug Cetrizine HCl in aqueous solutions of different concentrations and at different temperatures.

Conc. (M)	Adiabatic compressibility ($\beta a X 10^{-10}$) (m^2N^{-1})				Acoustic Impedance ($Z X 10^6$) (Nm^{-2})			
	298.15	303.15	308.15	313.15	298.15	303.15	308.15	313.15
0.02	4.17401	4.13822	4.10296	4.07079	1.547359	1.552918	1.558455	1.562972
0.04	4.15218	4.11348	4.07851	4.04401	1.552487	1.558652	1.564194	1.569727
0.06	4.1236	4.08894	4.05427	4.02008	1.558926	1.564396	1.569941	1.575474
0.08	4.09949	4.06567	4.03234	3.99949	1.564576	1.569738	1.57487	1.579979
0.1	4.07504	4.04665	4.00615	3.97965	1.570337	1.5745	1.581551	1.584254

Table no-5: Intermolecular free length (L_f) (nm) of Drug Cetrizine HCl in aqueous solutions of different concentrations and at different temperatures.

Concentration (M)	Intermolecular free length (L_f) (nm)			
	298.15	303.15	308.15	313.15
0.02	4.037913	4.059162	4.112288	4.15356
0.04	4.027339	4.04701	4.10002	4.139876
0.06	4.013454	4.034919	4.087818	4.127605
0.08	4.001702	4.023418	4.076747	4.117025
0.1	3.989751	4.013999	4.063485	4.106798

Table no-4 showsadiabatic compressibility (β) of the solution versus molarity (c) of the solution at temperatures of 298.15K, 303.15K, 308.15K and 313.15K. It is seen from this table that the value of adiabatic compressibility decreases with the increase of solute concentration for all the systems. The decrease of adiabatic compressibility with increasing concentration might be due to aggregation of solvent molecules around solute molecules indicating thereby the presence of solvent-solute interactions in all these systems. Similar decrease in adiabatic compressibilty has also been reported by M. Selvakumar et.al in solutions of Polymethyl methacrylate & polyethyleneglycol in tetrahydrofuran**.**[14] For a particular concentration adiabatic compressibility also decreases with increase in temperature. Table no-4 also depicts the variation of acoustic impedance (Z) of solution as a function of molarity (c) of solution at different temperatures. The acoustic impedance increases with increase in solute concentration. The acoustic impedance also increases with increase in temperature. Theoretical requirement of Z is density and velocity which are increased with increase of concentration of solute in solution. The increase of Z with solute concentration can be attributed to the effective solvent-solute interactions. Similar increase in acoustic impedance has also been reported by B. R. Shinde et.al in aqueous manganous chloride solution at different temperatures**.**[15]

Table no-5represents the values of intermolecular free length (Lf) of the solution at different concentration and at different temperatures. Lf decreases continuously which suggest that there is strong interaction between solvent and drug molecules. Similar decrease in intermolecular free length has also been reported by J. D. Pandey et.al during the study of Intermolecular free length and free volume of pure liquids at varying temperatures and pressures**.**[16]

III. Conclusion

In the present study, physicochemical properties of aqueous solutions of Cetrizine HCl in aqueous system at different temperatures are systematically presented. It has been observed that there exist strong solute–solvent interactions in these systems, which increases with increase in drug concentration. The values of Φv are positive suggest strong ion-solvent interactions. The positivevalues of Jones-Dole coefficient 'β' indicates structure promoting tendency and strong interactions between solute and solvent. Positive values of 'β' suggesting strongly hydrated solute indicating structure promoting tendency i.e. kosmotropes (structure makers).

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