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Density, Viscosity and Refractive Index Studies of Metformin HCl in Aqueous System at 303.15K.

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Abstract: - Density, Viscosity and Refractive Index of drug molecule Metformin HCl (MFH) in aqueous solution at different concentrations have been determined. The density, viscosity and refractive index data have been analyzed for the evaluation of apparent molar volume, molar excess volume, excess viscosity, specific refraction and molar refraction. It can be inferred from these studies that this drug acts as a structure-making compound due to hydrophobic hydration of drug molecules. B-coefficients values are found to be positive thereby showing solute-solvent interactions. Furthermore these results are correlated to understand the solution behavior of drug.

Keywords*: - Apparent molar volume, Excess Viscosity, Metformin HCl (MFH), Molar refraction.*

I. INTRODUCTION

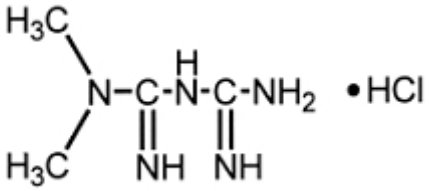
Drug-macromolecular interactions are an important phenomenon in physiological media, such as blood, membranes, intra- and extracellular fluids. The processes of drug transport, protein-binding, anesthesia are few examples where drug and bio-macromolecules appear to interact in an important and vitally significant manner. The mechanisms of these molecular processes, however, are not clearly understood. Because of the complexities associated with the structure of bio-macromolecules, or with the interpretation of their data, it is generally difficult to carry out direct studies of the physiological media.

The physicochemical properties of drug like density, viscosity and refractive index are strictly related to the molecular interactions taking place in the aqueous system [1].These interactions decides the drug actions i.e. drug reaching to the blood stream its extent of distribution, its binding to receptors and producing physiological actions [2].The interactions are of different types such as ionic or covalent, charge transfer, hydrogen bonding, ion-dipole and hydrophobic interactions. There are various papers appeared recently which use viscometric method to access thermodynamic parameters of bio-molecule and interpreted the solute-solvent interactions [3-5].Therefore we have decided to study the density, viscometric properties and refractive index of drug Metformin HCl in aqueous system at temperature of 303.15K. Metformin HCl is chemically 1, 1-Dimethylbiguanide hydrochloride. It is a white and crystalline powder. It is hygroscopic. It is freely soluble in water, slightly soluble in ethanol (95%), practically insoluble in acetone, chloroform, dichloromethane and in ether.

1.1. Drug profile

Molecular formula- $C_4H_{11}N_5.HCl$

Structure-



IUPAC name- 1,1-Dimethylbiguanide hydrochloride.
Molecular weight- 165.663g/mol
Category- Hypoglycaemic.
Solubility- It is freely soluble in water, slightly soluble in ethanol (95%), practically insoluble in acetone, chloroform, dichloromethane and in ether.

II. EXPERIMENTAL

2.1 Material

Double distilled water is used for preparation of solution mixture. The density, viscosity and refractive index of water are measured at 303.15K and compared with literature values.

2.2 Density

Densities of aqueous solutions of drug having different concentration were measured at 303.15K by using highly sophisticated Anton-paar densitometer at School of Chemical Sciences, North Maharashtra University, Jalgoan. A single pan electronic balance [*Sansui*; model KD-UBED of capacity 120 gm and with a precision of 0.0001 gm] was used for weighing purpose. The weighing was repeated thrice to ensure the accuracy in weights with a little interval of time. The reproducibility of the result was close to hundred percent. Viscosity measurements were carried out using Mansing Survismeter. The Refractive Index was measured by using Abbe Refractometer. The instrument is capable of determining refractive indices in the range of 1.3000 to 1.7000.

In the present work densities of drug molecule Metformin HCl in aqueous solution having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, 0.1M at different temperature of 303.15K were measured with Anton Paar Densitometer at School of Chemical Sciences, North Maharashtra University, Jalgoan. 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 density of standard solvent (double distilled water) was also measured at different temperatures and is found to be very close to the literature values.

Table 1. Density of water at different temperature

Sr. No.	Temperature (K)	Observed value (g.cm^{-3})	Literature value (g.cm^{-3})
1	298.15	0.997042	0.997045
2	303.15	0.995629	0.995647
3	308.15	0.994369	0.994032
4	313.15	0.992548	0.992216

Table 2. Density (ρ), Apperent molar volume (Φv) and Partial molar volume (Φ^0v) of MFH in Aqueous system at 303.15K.

Concentration (M)	Density (g cm^{-3})	Φv (cm^3 mol^{-1})	Φ^0v
0.02	0.996178	147.9715	141.4387
0.04	0.996674	149.3265	
0.06	0.997170	151.2368	
0.08	0.997666	153.2687	
0.1	0.998162	155.2987	

2.3 Viscosity

Viscosity measurements were carried out by using Mansing Survismeter. The temperature was controlled by water-bath, whose temperature was maintained constant at 303K (± 0.01°C). A fixed volume (15ml) of the solution was delivered into the viscometer. The viscometer was kept for 20 minutes in the thermostatically controlled water-bath to achieve constant temperature.

The experimental measurements of viscous flow time (VFT) of the solution between two points on the viscometer were performed at least three times for each solution and the average results were noted.

Table 3. Viscosity (Nsm^{-2}), Relative Viscosity (Nsm^{-2}) and Excess Viscosity of Metformin HCl in Aqueous system at 303.15K.

Concentration (M)	Viscosity (N s m^{-2})	Relative Viscosity (N s m^{-2})	Excess viscosity (mPas)
0.02	0.802014	1.006291	1.59841
0.04	0.816587	1.024576	1.61236
0.06	0.823284	1.032979	1.61852
0.08	0.853493	1.070882	1.64807
0.1	0.868847	1.090147	1.66286

2.4 Refractive Index

The refractive index of drug Metformin HCl in aqueous solution having concentrations of 0.02M, 0.04M, 0.06M, 0.08M, 0.1M at temperatures of 303K. Refractive Indices measurements were made on Abbe refractometer [make-optics technology]. The temperature was maintained by circulating water through jacket around the prisms of refractometer from an electronically controlled heated bath circulator (MAC-MSW-270). The uncertainty of temperature was ± 0.01^{o}C. The refractive index was measured by using Na- vapour lamp with wavelength of D-line of Na is 589.3 nm. [6]A small quantity of the experimental liquid is introduced between the two prisms. The reflector fitted on the base of the instrument is adjusted in such a way that a beam of light passes through the opening at the bottom of the lower prism. The eyepiece of telescope is focused on the cross-wire in its focal plane. The prism chamber is rotated by operating the milled head until the cross-wire coincides with the line of demarcation between bright and dark halves of the field of view. At this position, the reading on the scale directly gives the value of refractive index of the liquid. The calibration of the refractometer was made by measuring the refractive indices of standard liquids viz. benzene and carbon tetra chloride at 298K. Refractive indices were found to be 1.501 and 1.461 respectively which are very close to the respective literature values [7] of 1.5011 and 1.4607. Refractive index of double distilled water was measured at temperature range of 25^{0}C (298K) to 40^{0}C (313K) and it was compared with literature.

Table 4.Refractive Index of water at different temperatures.

Sr. No.	Temperature (K)	Observed value	Literature value
1	298.15	1.3325	1.33254
2	303.15	1.33186	1.33192
3	308.15	1.33128	1.33134
4	313.15	1.33112	1.33124

Table 5. Refractive Index, Molar refraction and Specific Refraction (R_S) of MFH in Aqueous system at 303.15K

Concentration (M)	Refractive Index (n_D)	Molar refraction (R_M)	Specific Refraction (R_S)
0.02	1.33325	34.23018	0.206625
0.04	1.3333	34.2178	0.206551
0.06	1.33335	34.20544	0.206476
0.08	1.3334	34.19309	0.206401
0.1	1.33345	34.18075	0.206327

III. RESULTS AND DISCUSSION

The densities, viscsity and refractive indices of Metformin HCl in aqueous system at different concentrations and at temperature of 303.15K were measured. These physicochemical properties were further used for determination of different thermodynamic properties. The apparent molar volume Φv was obtained from density using following equation

$$\Phi v = \frac{1000}{C} \times \frac{d0 - d}{d0} + \frac{M}{d0}$$

where *do* is the density of pure solvent(water) d is the density of solution, c is molar concentration, M is molar mass of drug.

The values of the densities (ρ) and apparent molar volumes (Φv) of Metformin HCl in aqueous system at different concentrations and at temperature of 303.15K are shown in table no-2. The table no-2 reveals that densities and apparent molar volumes (Φv) of Metformin HCl solutions under investigation increases with increase in concentration. Such observations were previously made by Comesana et al,Lee et .al ,and Nikumbh et al for other solutions.[8-11]

The apparent molar volumes (Φv) were plotted against the square root of concentration (C½) in accordance with the Masson's equation--- $\Phi v = \Phi v^{0} + Sv.C^{½}$, where Φv^{0} is the partial molar volume and Sv a semi-empirical parameter which depends on the nature of solvent, solute and temperature.

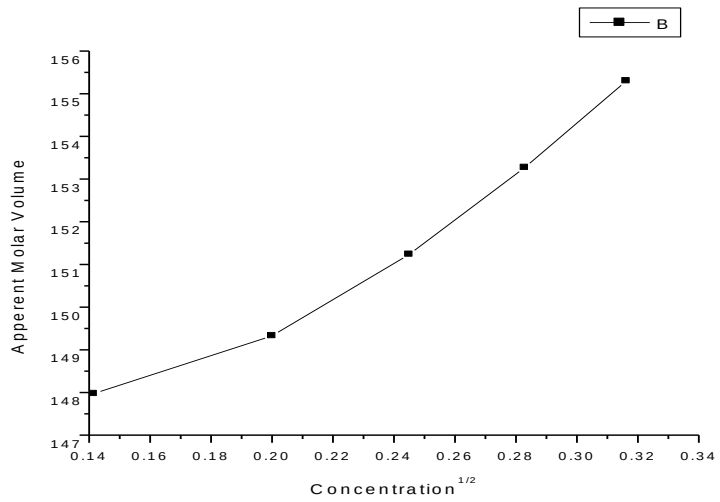


Figure 1. Variation of Apparent Molar Volume with Concentration.

The refractive indices n_D of drug MFH at different concentrations investigated in this work are reported in table V. Molar refractivity and Spcific refraction also reported in table V, was obtained from n_D experimental data according to the following expression:

$$R = \left[\frac{\eta_D^2 - 1}{\eta_D^2 + 2}\right] + \frac{M}{d}$$

Where , M is the molecular weight of the drug and d is the mixture density.

The measured values of viscosities and relative viscosities of aqueous solution of drug Metformin HCl having different concentrations are mentioned in table no-3. Table no-3 reveals that viscosities and relative viscosities increase with increase in concentration at particular temperature. The values of viscosity were used to calculate the excess viscosity ηE of the liquid mixtures using the formula----ηE = ηmix –(x1η1 - x2η2) where, ηmix, η1 and η2 are the viscosities of liquid mixtures, component 1 and 2 respectively and x1 and x2 are the mole fractions of component 1 and 2 respectively. The calculated values of excess viscosity (ηE) are given in table no-3.The trend of excess viscosity shows that these values increase with increase in concentration of solution. Similar trend in excess viscosity for some drug was observed by Farooqui et.al.[12]. Arbad et.al.[13] measured the excess viscosity of the natural macromolecules in alcohol-water mixtures at different temperature and also reported the same results.

The variation of excess viscosity with concentration is shown in Fig no-2.

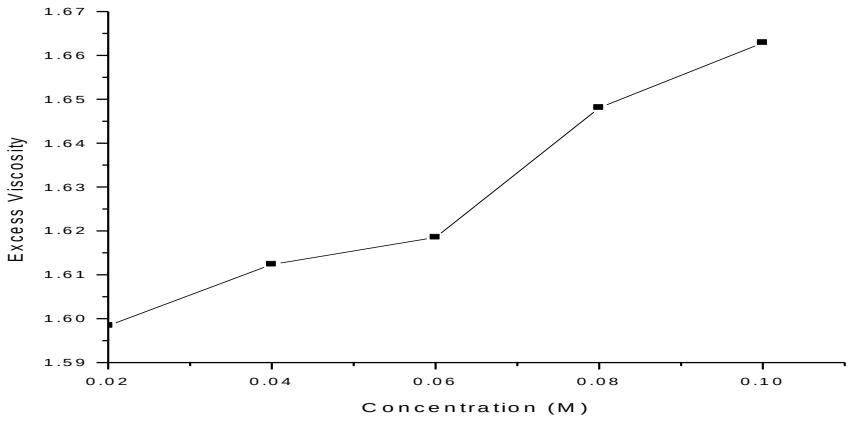


Figure 2. Variation of excess viscosity with concentration.

IV. CONCLUSION

In the present study, physicochemical properties of drug Metformin HCl in aqueous solution of different concentration at 303.15 K temperature 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 and all other physico-chemical properties are positive which suggest strong solute-solvent interactions. The values of all physico-chemical properties increases with increase in concentration, this suggests that Metformin HCl is a structure making molecules.

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