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The study of Apparent Molar Volume and Adiabatic Compressibility of and Metformin HCl and Trandolapril in Aqueous Solvent Systems at Different Temperatures.

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ABSTRACT

The study of the physicochemical properties of Trandolapril and Metformin HCl as electrolytes in solution provides information useful to elucidate ion–ion, ion–solvent, and solvent–solvent interactions. Apparent molar volumes (Φv), and adiabatic compressibility for Trandolapril and Metformin HCl in aqueous system have been determined from density (ρ) and viscosity (η) measurements at four different temperatures. 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: Trandolapril, Metformin HCl, density, viscosity, adiabatic compressibility.

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. 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].

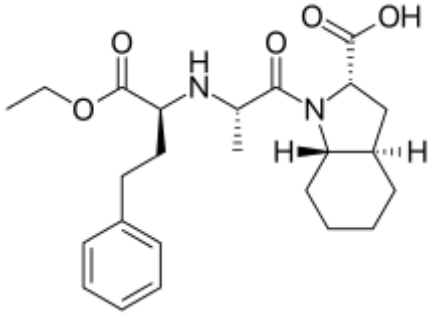
DRUG PROFILE

1. Trandolapril

Molecular formula- $C_{24}H_{34}N_2O_5$

Molecular weight- 430.50 g/mol

Structure-



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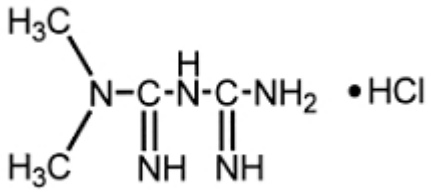
IUPAC name- (2S, 3R, 7S)-1-[(S)-1-(ethoxycarbonyl)-3-(phynyl-propylamino)-1-oxo-propyl] octahydro-1H-Indole-2-carboxylic acid.
Category- Antihypertensive.
Solubility- Sparingly soluble in water and soluble in methanol.

2. Metformin HCl

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.

EXPERIMENTAL

Materials:

Drugs of high purity were 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 drugs Trandolapril and Metformin 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.

Viscosity measurements:

The aqueous solutions of drugs Trandolapril and Metformin HCl having 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 temperature was maintained by circulating water through Mansing Survismeter from an electronically controlled heated bath circulator (MAC-MSW-270). The uncertainty of temperature was ± 0.01^oC.

Ultrasonic Velocity measurements:

In the present work, the ultrasonic velocity measurements of drugs Trandolapril and Metformin 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.

The temperature was maintained by circulating water around the liquid cell from thermostatically controlled adequately stirred water bath (accuracy + 0.1^oC) and covering the measuring cell along with its base with a specially made insulated jacket with a window for noting down micrometer readings.

Data Evaluation:

The apparent molar volumes, (Φ_v) were obtained from the density results using the following equation -1.

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

Where M= molar mass of drug, C= concentration in mol.L^{-1} , d= densities of the solution and d_0= density of the solvent.

From the value of viscosity, relative viscosity (η_r) is calculated by using following equation-

$\eta r = (\eta/\eta_o)$ where η are η_o are viscosities of the solution and solvent respectively.

The adiabatic compressibility (β_S) of a liquid is related to ultrasonic velocity (U) for a liquid of density d_s by an equation-

$$\beta_S = 100/U^2 \times d_s$$

RESULTS AND DISUSSION

The values of the densities (ρ), viscosity, Ultrasonic velocity, apparent molar volumes (Φv), relative viscosities and adiabatic compressibility of drugs Trandolapril and Metformin HCl Cetrizine HCl in aqueous solution at different temperatures are shown in table no-1 to table no-3.

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

Drug molecules		Density ($g.cm^{-3}$)				Apparent molar volumes (Φv)			
1.Metformin HCl	**Temp. (K) →** / **Conc^n (M) ↓**	**298.15**	**303.15**	**308.15**	**313.15**	**298.15**	**303.15**	**308.15**	**313.15**
	0.02	0.99758	0.99617	0.99455	0.99272	138.974	147.971	157.349	167.259
	0.04	0.99808	0.99667	0.99504	0.99321	140.002	149.326	159.327	169.864
	0.06	0.99858	0.99717	0.99553	0.99370	142.364	151.236	161.289	171.268
	0.08	0.99908	0.99766	0.99602	0.9941	144.553	153.267	163.257	173.249
	0.1	0.99958	0.99816	0.99651	0.99467	146.326	155.298	165.230	175.477
2.**Trandolapril**	0.02	0.99829	0.99730	0.99630	0.99460	368.790	350.2489	335.438	326.315
	0.04	0.99897	0.99797	0.99698	0.99598	378.409	360.4574	345.268	336.136
	0.06	0.99964	0.99865	0.99765	0.99667	388.265	371.5678	356.870	346.499
	0.08	1.00031	0.99932	0.99832	0.99733	396.706	382.0125	365.170	355.407
	0.1	1.00099	0.99999	0.99900	0.99801	402.458	388.5182	374.208	361.641

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Table 2: Viscosities and Relative Viscosities of Metformin HCl and Trandolapril in aqueous solutions of different concentrations and at different temperatures.

Drug molecules		Viscosities				Relative Viscosities			
1.Metformin HCl	**Temp. (K) →** / **Conc^n (M) ↓**	**298.15**	**303.15**	**308.15**	**313.15**	**298.15**	**303.15**	**308.15**	**313.15**
	0.02	0.9112	0.8020	0.7265	0.6877	1.0227	1.0062	1.0105	1.00548
	0.04	0.9426	0.8165	0.7488	0.6998	1.0579	1.0245	1.0415	1.0232
	0.06	0.9622	0.8232	0.7597	0.7132	1.0799	1.0329	1.0567	1.0428
	0.08	0.9758	0.8534	0.7733	0.7359	1.0952	1.0708	1.0755	1.0759
	0.1	0.9935	0.8688	0.7848	0.7569	1.1150	1.0901	1.0916	1.1067
2.**Trandolapril**	0.02	0.9902	0.8939	0.8611	0.8365	1.1113	1.1216	1.1976	1.2230
	0.04	1.0163	0.9146	0.8813	0.8543	1.1406	1.1476	1.2257	1.2490
	0.06	1.0358	0.9378	0.9064	0.8730	1.1625	1.1766	1.2607	1.2764
	0.08	1.0591	0.9580	0.9290	0.8947	1.1887	1.2020	1.2920	1.3080
	0.1	1.0746	0.9789	0.9495	0.9173	1.2060	1.2282	1.3205	1.3411

Table 3: Ultrasonic Velocities ($m.s^{-1}$) and Adiabatic Compressibility of Metformin HCl and Trandolapril in aqueous solutions of different concentrations and at different temperatures.

Drug molecules		Ultrasonic Velocities ($m.s^{-1}$)				Adiabatic compressibility (m^2N^{-1})			
1.Metformin HCl	**Temp. (K) →** / **Conc^n (M) ↓**	**298.15**	**303.15**	**308.15**	**313.15**	**298.15**	**303.15**	**308.15**	**313.15**
	0.02	1500.9	1512.3	1524	1533	4.4498	4.3892	4.3291	4.2863
	0.04	1502.4	1513.8	1527.6	1536.3	4.4387	4.3783	4.3066	4.2658
	0.06	1504.2	1514.7	1531.5	1540.2	4.4259	4.3709	4.2826	4.2421
	0.08	1505.4	1515.9	1535.4	1543.8	4.4166	4.3618	4.2587	4.2203
	0.1	1506.9	1517.1	1539	1547.4	4.4056	4.3528	4.2368	4.1986
2.**Trandolapril**	0.02	1527.9	1534.8	1541.7	1548.6	4.2909	4.2566	4.2228	4.1925
	0.04	1530.6	1537.5	1544.4	1551.3	4.2729	4.2388	4.2052	4.1721
	0.06	1533.6	1540.5	1547.4	1554.6	4.2533	4.2194	4.1861	4.1517
	0.08	1536	1543.2	1550.4	1556.4	4.2372	4.2019	4.1671	4.1391
	0.1	1538.7	1546.6	1552.8	1559.7	4.2195	4.1806	4.1514	4.1188

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Table no-1 reveals that densities of Metformin HCl and Trandolapril solutions 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 Φv increases with increase in concentration. The Φv values are large and positive suggests presence of strong solute-solvent interactions promotes 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] Table no-3 also shows adiabatic 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[13]. For a particular concentration adiabatic compressibility also decreases with increase in temperature.

CONCLUSION

In the present study, physicochemical properties of Metformin HCl and Trandolapril 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. Positive values of 'β' suggesting strongly hydrated solute indicating structure promoting tendency i.e. kosmotropes (structure makers).

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