

# Ultrasonic Study of Molecular Interactions in Aqueous Solution of Valganciclovir-HCl

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**ABSTRACT:** Valganciclovir-hydrochloride drug is a drug used for the treatment of Cyto MegaloVirus (CMV) retinitis (a viral infection and inflammation of the eye's retina) in adults with AIDS. Molecular interactions of Valganciclovir-hydrochloride with distilled water have been investigated using experimental and computational techniques. The drug has been added in specific quantities to distilled water to obtain certain molarity mixture solutions ranging from 0.025M to 0.3M. 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 303 K to 318 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:** Valganciclovir hydrochloride, Ultrasonic Studies, Inter Molecular interactions.

## I. INTRODUCTION

Pharmaceutical and medicinal industry seek understanding of a drug's physico-chemical behaviour 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[1,2]. 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 across the biological membranes[3,4]. As there is demand from a local pharmaceutical company to study the interaction of valganciclovir-HCl with distilled water, we studied the drug's interaction with distilled water.

Valganciclovir is the generic name of the drug which is chemically designated as [2-[(2-amino-6-oxo-3H-purin-9-yl)methoxy]-3-hydroxypropyl](2S)-2-amino-3-methylbutanoate. The trade or brand name of it is "Valcyte". The drug is used to for the treatment of Cyto Megalovirus (CMV) retinitis in adults with AIDS. Its chemical formula is  $C_{14}H_{22}N_6O_5$ . Valcyte is often formulated as the Hydrochloride salt. Its formula is  $C_{14}H_{22}N_6O_5 \cdot HCl$  (or  $C_{14}H_{23}ClN_6O_5$ ) representing a molecular weight of 390.822 g/mole. For completeness and forthcoming understanding of Valcyte's interaction with the distilled water its molecular structure has been shown in Fig.1.

In the present paper, we present the results obtained for experimental and computational study for understanding the intermolecular interactions of the Valcyte with distilled water for different concentrations and at different temperatures. We limited our study to the temperature range of 303K to 318 K. Experimental methods used for measuring density ( $\rho$ ), viscosity ( $\eta$ ) 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. From the nature of variation of these measured and derived

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parameters with concentration and temperature, the strength of interaction of the solute with the solvent has been deduced and explained.

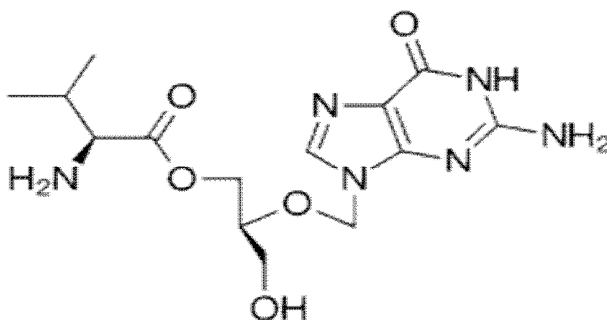


Fig. 1 Molecular Structure of Valganciclovir

## II. EXPERIMENTAL AND COMPUTATIONAL TECHNIQUES

### Materials

The drug Valganciclovir-Hydrochloride (CAS No. 175865-59-5, minimum assay value 99%) has been used in this study. All the mixtures were prepared in double distilled water on a molarity basis by using Digital Balance with an accuracy of  $\pm 0.1$  mg. The concentration of the drug-distilled water mixture has been varied in the range 0.025 M to 0.3 M.

### Experimental Methods

Standard experimental techniques [5-14] have been used for measurement of density, viscosity and ultrasonic velocity in the mixture solution at different temperatures. The density ( $\rho$ ) of the mixture solutions have been measured using a specific gravity bottle at temperatures 303.15 K, 308.15 K, 313.15 K, 318.15 K. The accuracy in the density measurements is about  $\pm 0.0001$  g/ml. The viscometric measurements have been made by Ostwald's Viscometer with an accuracy of 0.001 N.s.m<sup>-2</sup>. The viscosity of the mixture solution has been obtained used the equation

$$\eta = \eta_s \frac{\tau}{\tau_s} \frac{\rho}{\rho_s} \quad (1)$$

where  $\eta$ ,  $\rho$  and  $\tau$  represent the viscosity, density and time of flow in Ostwald's viscometer. Quantities without subscript are for mixture solution and those with subscript 's' are for the solvent.

The ultrasonic velocity (U) in the mixture has been measured by using variable path single crystal interferometer (Model F-81S, Mittal Enterprises, India) at a fixed frequency of 2 MHz with an accuracy of 0.03%. The temperature has been maintained with an accuracy of 0.1 °C by a water thermostat (Thermal Instruments & Equipments). For low temperature bath model, LTB-10 was used to circulate water through the double walled measuring cell made up of steel containing the experimental solution to attain the desired temperature. This device can be used for temperatures between -10 °C to 90 °C.

### Analytical/Computational Methods

We have developed a Fortran code called CIMIUS (Code for Intermolecular Interactions using Ultrasonic Studies). This software uses the measured values of density ( $\rho$ ), viscosity ( $\eta$ ) and sound velocity (U) at difference concentrations and temperatures and computes the certain quantities based on which the nature of the intermolecular interactions

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between the solute (Valcyte) and the solvent (Distilled Water) can be found out. The derived parameters are as listed below:

Adiabatic compressibility ( $\chi$ ) is a measure of the amount of compression that can be achieved in a material. Hence, it is also a good measure of how strong the intermolecular interactions are in the solution.  $\chi$  of mixture solution can be computed from

$$\chi = \frac{1}{\rho U^2} \quad (2)$$

Intermolecular free length ( $L_f$ ) is the average distance between surfaces of neighbouring molecules. The variation of  $L_f$  with the concentration of the solution and temperatures would reveal the strength of the intermolecular interactions.  $L_f$  for a mixture can be obtained from

$$L_f = K_T \chi^{1/2} \quad (3)$$

where  $K_T$  is a temperature dependent constant which is  $205.8336 \times 10^{-8}$  (SI units).

Similarly, free volume ( $V_f$ ) is the volume in which an individual molecule moves in an average potential due to its neighbours.  $V_f$  of a mixture solution can be obtained from

$$V_f = \left( \frac{M_{eff} U}{\eta K} \right)^{3/2} \quad (4)$$

where  $K$  is constant equal to  $4.28 \times 10^9$  (SI units).  $M_{eff} = \sum m_i x_i$ , where  $m_i$  and  $x_i$  are Molecular weight and mole fractions of the component 'i'.

Acoustic impedance can be computed by

$$Z = \rho U \quad (5)$$

Relaxation time ( $\tau$ ) is the time taken for excitation energy to appear as translational energy and it depends on the temperature and impurities. This is also a measure of strength of intermolecular interaction.  $\tau$  can be computed as

$$\tau = \frac{4}{3} \eta \chi \quad (6)$$

Molar Volume ( $V$ ) of the solution can be calculated from

$$V = \frac{M_{eff}}{\rho} \quad (7)$$

Vander Waals constant (b) can be calculated from

$$b = \frac{M_{eff}}{\rho} \left[ 1 - \left( \frac{RT}{M_{eff} U^2} \right) \left\{ \left( 1 + \frac{M_{eff} U^2}{3RT} \right)^{1/2} - 1 \right\} \right] \quad (8)$$

where  $R$  is the gas constant ( $= 8.314$  J/K/mole) and  $T$  is the temperature.

Internal pressure ( $\Pi$ ) in the mixture is a cohesive force, which is a resultant of forces of attraction and forces of repulsion between molecules. Dissolved solutes exist under the internal pressure of medium and their interactions with the solvent, in general, arise through H-bonding, charge transfer, Columbic or Vanderwaal's interactions. Hence,  $\Pi$  is also a measure of the strength of intermolecular interactions in a mixture solution and can be computed from

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$$\Pi = BRT \left( \frac{k\eta}{U} \right)^{1/2} \frac{\rho^{3/2}}{M_{eff}^{7/6}} \quad (9)$$

where B is the packing factor which is 2.

Enthalpy of the medium can be given by

$$H = \Pi V \quad (10)$$

where V is the molar volume given by  $M_{eff}/\rho$ .

Rao's constant or Molar sound velocity can be computed from

$$R = U^{1/3} V \quad (11)$$

Wada's constant or Molar compressibility can be computed from

$$W = \chi^{-1/7} V \quad (12)$$

The relative association (RA) can be calculated from

$$RA = \frac{\rho}{\rho_s} \left( \frac{U_s}{U} \right)^{1/3} \quad (13)$$

### III. RESULTS AND DISCUSSION

Tables 1 to 4 list the measured and derived parameters using CIMIUS code for Valcyte-Distilled water mixtures for different concentrations of the solution and at different temperatures.

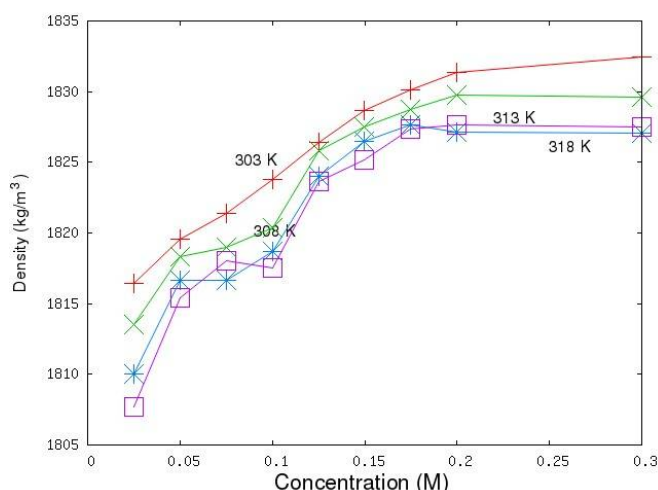


Fig. 2 Measured Density of Valcyte -Distilled water solution at different Concentrations and Temperatures

Fig. 2 shows the variation of density of the drug solution with concentration at different temperatures. The density of the solution increases rapidly with concentration and appears to saturate at high concentrations. Since, the volume of the solution is equal in all the cases; the increase in the density indicates increasing number of molecules per unit volume. Hence, this indicates strong interaction between solute-solvent molecules. As the temperature increases, the density decreases as a result of increase in various bond lengths.

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Table 1. Measured density, Sound speed and Viscosity values of Valcyte-Distilled water Solution at different Concentrations and Temperatures

Temperature (K)	Concentration (M)	Density (kg/m <sup>3</sup> )	Sound Speed (km/s)	Viscosity (x 10 <sup>-3</sup> Pa-sec)
<b>303</b>	0.025	1816	1.5235	2.2999
	0.05	1819	1.524	2.32061
	0.075	1821	1.531	2.35635
	0.1	1823	1.539	2.37622
	0.125	1826	1.545	2.39640
	0.15	1828	1.556	2.43288
	0.175	1830	1.564	2.45160
	0.2	1831	1.6117	2.47006
	0.3	1832	1.612	2.48835
<b>308</b>	0.025	1813	1.524	2.14649
	0.05	1818	1.5245	2.18560
	0.075	1818	1.535	2.21971
	0.1	1820	1.545	2.27154
	0.125	1825	1.549	2.31182
	0.15	1827	1.561	2.33074
	0.175	1828	1.569	2.34908
	0.2	1829	1.6125	2.35036
	0.3	1829	1.6127	2.36699
<b>313</b>	0.025	1810	1.5245	2.00949
	0.05	1816	1.525	2.06685
	0.075	1816	1.540	2.10021
	0.1	1818	1.551	2.13593
	0.125	1824	1.556	2.17565
	0.15	1826	1.566	2.22888
	0.175	1827	1.585	2.26385
	0.2	1827	1.613	2.27994
	0.3	1827	1.614	2.27984
<b>318</b>	0.025	1807	1.525	1.82446
	0.05	1815	1.5255	1.86553
	0.075	1818	1.543	1.91831
	0.1	1817	1.562	1.95111
	0.125	1823	1.563	1.99115
	0.15	1825	1.574	2.04308
	0.175	1827	1.592	2.04554
	0.2	1827	1.6135	2.04580
	0.3	1827	1.614	2.06244

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Table 2. Computed values of Compressibility, Impedance, Free-length and Free-Volume of Valcyte-Distilled Water Solution at different Concentrations and Temperatures

Temperature (K)	Concentration (M)	Compressibility ( $\times 10^{-10} \text{ Pa}^{-1}$ )	Acoustic Impedance ( $\times 10^6 \text{ kg/m}^2/\text{s}$ )	Free Length ( $\times 10^{-10} \text{ m}$ )	Free Volume ( $\times 10^{-8} \text{ m}^3/\text{mole}$ )
<b>303</b>	0.025	2.37194	2.76729	0.317006	0.472827
	0.05	2.36625	2.77303	0.316626	0.473928
	0.075	2.34233	2.78854	0.315021	0.473492
	0.1	2.31496	2.80685	0.313175	0.478346
	0.125	2.29371	2.82185	0.311735	0.482180
	0.15	2.25864	2.84540	0.309343	0.483468
	0.175	2.23382	2.86230	0.307638	0.488687
	0.2	2.10213	2.95159	0.298433	0.512826
	0.3	2.10009	2.95391	0.298288	0.536686
<b>308</b>	0.025	2.37416	2.76379	0.317155	0.524670
	0.05	2.36627	2.77209	0.316627	0.518771
	0.075	2.33322	2.79213	0.314409	0.519909
	0.1	2.30133	2.81250	0.312252	0.514785
	0.125	2.28266	2.82818	0.310983	0.510860
	0.15	2.24561	2.85275	0.308449	0.518081
	0.175	2.22128	2.86929	0.306773	0.523524
	0.2	2.10190	2.95045	0.298416	0.552906
	0.3	2.10152	2.95062	0.298389	0.578864
<b>313</b>	0.025	2.37719	2.75936	0.317357	0.579515
	0.05	2.36697	2.77037	0.316674	0.564393
	0.075	2.32105	2.79766	0.313587	0.567671
	0.1	2.28570	2.82078	0.311190	0.567875
	0.125	2.26440	2.83816	0.309737	0.563360
	0.15	2.23254	2.86028	0.307550	0.556661
	0.175	2.17794	2.89685	0.303766	0.561850
	0.2	2.10361	2.94713	0.298538	0.578991
	0.3	2.10109	2.94884	0.298359	0.613111
<b>318</b>	0.025	2.37869	2.75672	0.317457	0.670201
	0.05	2.36706	2.76935	0.316680	0.658497
	0.075	2.31028	2.80523	0.312859	0.652199
	0.1	2.25507	2.83895	0.309098	0.657376
	0.125	2.24462	2.85035	0.308381	0.647796
	0.15	2.21148	2.87285	0.306096	0.639163
	0.175	2.15915	2.90920	0.302453	0.658492
	0.2	2.10173	2.94885	0.298404	0.681497
	0.3	2.10056	2.94958	0.298321	0.712566

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Table 3. Computed values of Relative Association, Viscous Relaxation Time, Molar Volume and Internal Pressure of Valcyte-Distilled water Solution at different Concentrations and Temperatures

Temperature (K)	Concentration (M)	Relative Association	Relaxation Time ( $\times 10^{-13}$ s)	Molar Volume ( $\times 10^{-2}$ lt/mole)	Internal Pressure (GPa)
<b>303</b>	0.025	1.79976	7.27363	1.00207	0.292675
	0.05	1.80270	7.32153	1.01057	0.298237
	0.075	1.80175	7.35912	1.01980	0.303839
	0.1	1.80101	7.33446	1.02866	0.308505
	0.125	1.80127	7.32885	1.03739	0.313472
	0.15	1.79920	7.32666	1.04632	0.318928
	0.175	1.79755	7.30191	1.05568	0.323349
	0.2	1.78084	6.92318	1.06514	0.323655
	0.3	1.78180	6.96769	1.10519	0.339658
<b>308</b>	0.025	1.79670	6.79480	1.00367	0.286679
	0.05	1.80131	6.89562	1.01124	0.293865
	0.075	1.79779	6.90545	1.02115	0.298779
	0.1	1.79530	6.97010	1.03060	0.305153
	0.125	1.79910	7.03612	1.03775	0.312406
	0.15	1.79615	6.97856	1.04698	0.316505
	0.175	1.79429	6.95727	1.05647	0.320865
	0.2	1.77898	6.58697	1.06608	0.320423
	0.3	1.77879	6.63237	1.10691	0.335884
<b>313</b>	0.025	1.79303	6.36924	1.00561	0.281020
	0.05	1.79940	6.52287	1.01220	0.289948
	0.075	1.79356	6.49959	1.02245	0.294301
	0.1	1.79131	6.50944	1.03156	0.299704
	0.125	1.79463	6.56873	1.03877	0.306839
	0.15	1.79323	6.63476	1.04757	0.313770
	0.175	1.78718	6.57404	1.05709	0.318203
	0.2	1.77625	6.39480	1.06761	0.319969
	0.3	1.77581	6.38688	1.10847	0.334152
<b>318</b>	0.025	1.79053	5.78642	1.00690	0.271479
	0.05	1.79795	5.88777	1.01291	0.279529
	0.075	1.79376	5.90912	1.02168	0.285807
	0.1	1.78594	5.86652	1.03223	0.289713
	0.125	1.79157	5.95917	1.03898	0.297469
	0.15	1.78891	6.02431	1.04831	0.304105
	0.175	1.78429	5.88885	1.05725	0.306558
	0.2	1.77655	5.73296	1.06732	0.308015
	0.3	1.77626	5.77637	1.10819	0.323020



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Table 4. Computed values of Rao's Constant, Wada's Constant, Vander Waals Constant and Enthalpy of Valcyte-Distilled Water Solution at different Concentrations and Temperatures

Temperature (K)	Concentration (M)	Rao's constant (lt/mole)(m/s) <sup>1/3</sup>	Wada constant (lt/mole) Pa <sup>1/7</sup>	Van der Waal constant (x 10 <sup>-3</sup> lt/mole)	Enthalpy (x 10 <sup>7</sup> J/mole)
<b>303</b>	0.025	0.115305	0.237621	9.08435	0.293282
	0.05	0.116295	0.239718	9.16449	0.301389
	0.075	0.117537	0.242259	9.25378	0.309855
	0.1	0.118764	0.244775	9.34020	0.317347
	0.125	0.119927	0.247177	9.42466	0.325193
	0.15	0.121246	0.249855	9.51293	0.333701
	0.175	0.122540	0.252487	9.60398	0.341353
	0.2	0.124883	0.256972	9.71111	0.344740
	0.3	0.129587	0.266671	10.0880	0.375389
<b>308</b>	0.025	0.115501	0.23796	9.09431	0.287731
	0.05	0.116385	0.239878	9.16607	0.297169
	0.075	0.117795	0.242715	9.26281	0.305099
	0.1	0.119142	0.245443	9.35525	0.314490
	0.125	0.120072	0.247433	9.42458	0.324199
	0.15	0.121452	0.250219	9.51596	0.331375
	0.175	0.122763	0.252880	9.60820	0.338985
	0.2	0.125014	0.257202	9.71502	0.341597
	0.3	0.129806	0.267059	10.0989	0.371792
<b>313</b>	0.025	0.115737	0.238385	9.10747	0.282597
	0.05	0.116509	0.240095	9.17032	0.293487
	0.075	0.118073	0.243206	9.27180	0.300909
	0.1	0.119408	0.245911	9.36154	0.309164
	0.125	0.120371	0.247961	9.43179	0.318735
	0.15	0.121650	0.250568	9.51841	0.328695
	0.175	0.123251	0.253742	9.61511	0.336371
	0.2	0.125206	0.257542	9.72431	0.341604
	0.3	0.130024	0.267443	10.1086	0.370397
<b>318</b>	0.025	0.115899	0.238670	9.11481	0.273354
	0.05	0.116602	0.240261	9.17230	0.283137
	0.075	0.118060	0.243183	9.26131	0.292003
	0.1	0.119767	0.246545	9.36709	0.299050
	0.125	0.120576	0.248323	9.43169	0.309065
	0.15	0.121944	0.251086	9.52350	0.318797
	0.175	0.123451	0.254095	9.61445	0.324109
	0.2	0.125185	0.257504	9.71704	0.328751
	0.3	0.129991	0.267385	10.1010	0.357967



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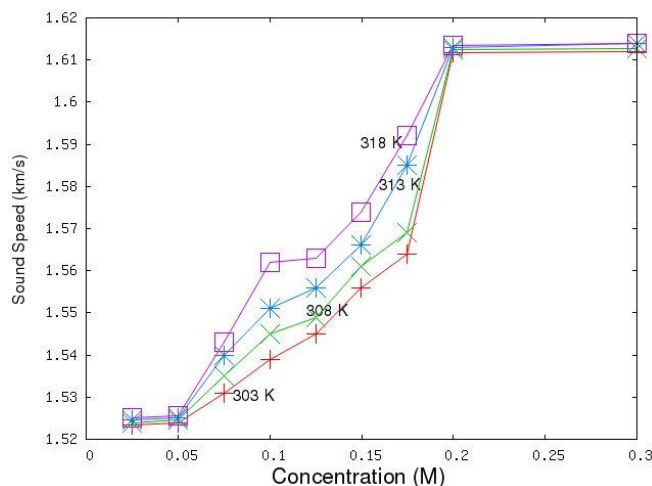


Fig. 3 Measured Sound Speed in Valcyte-Distilled water solution at different concentrations and Temperatures

Fig. 3 shows the variation of the sound speed in the solution with concentration and temperature. In general, the sound speed has been observed to be increasing linearly from 0.05M to 0.2M. This is consistent with the density variation and indicates strong intermolecular interactions between solute-solvent molecules. For a given concentration sound speed increases steadily with increase in temperature.

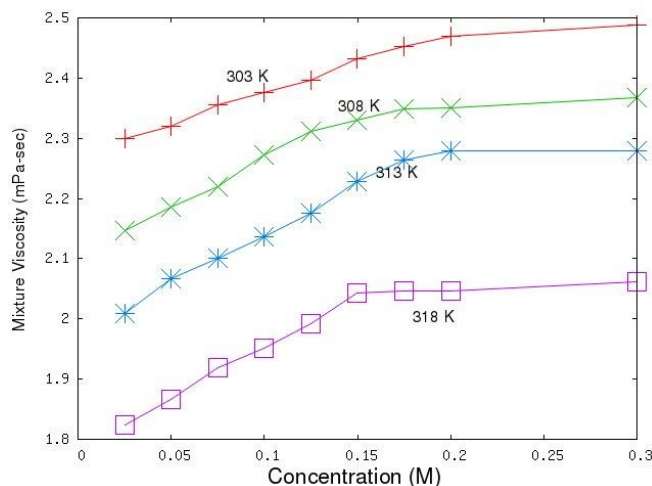


Fig. 4 Measured Viscosity of Valcyte-Distilled water solution at different concentrations and Temperatures

The variation of viscosity of the Valcyte –Distilled water solution with concentration and temperature has been shown in the fig. 4. It can be seen that the viscosity of the mixture solution increases with concentration in general. Viscosity is due to cohesive or shear forces between different molecules or layers in the solution. Hence, increase in the viscosity means enhancement of the cohesive forces between solute-solvent-solvent molecules, which again indicate the existence of strong intermolecular forces between solute-solvent molecules. At a given concentration, the viscosity decreases with increase in temperature, which is consistent with the density variation.

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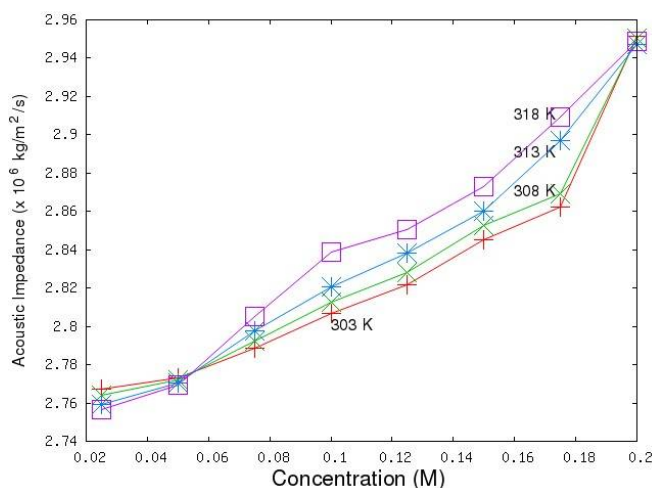


Fig. 5 Calculated Impedance of Valcyte-Distilled water solution at different concentrations and Temperatures

Acoustic impedance ( $Z$ ) is a measure of resistance of the medium to introduction of disturbances. This is equal to the product of density and sound speed of the medium. The amount of sound wave transmission or reflection at interfaces depends on the acoustic impedance of the medium. Hence,  $Z$  is an important parameter to be studied. Figure 5 shows the variation of  $Z$  with concentration and temperature of the solution.  $Z$  increases with the concentration at a given temperature and increases with temperatures at a given concentration. These trends are consistent with the density and sound speed variations.

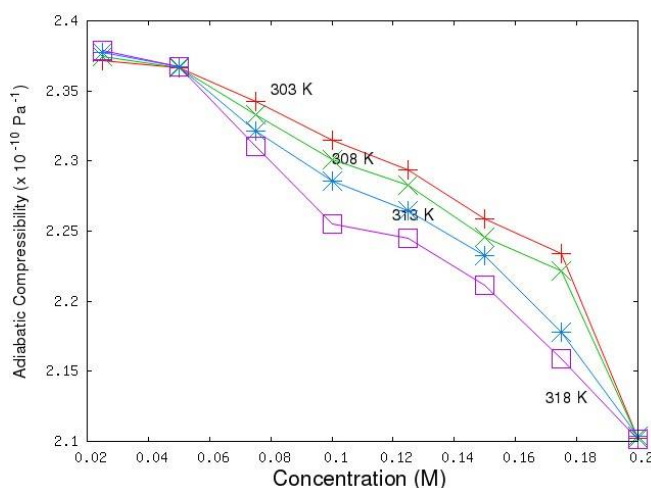


Fig. 6 Calculated Adiabatic Compressibility of Valcyte-Distilled water solution at different concentrations and Temperatures

Adiabatic compressibility ( $\chi$ ) is a measure of change in volume of the medium for applied pressure or forces. This is reciprocal of bulk modulus. Fig. 6 shows the variation of the adiabatic compressibility with concentration and temperature.  $\chi$  decreases as the concentration increases at a given temperature. It is due to the fact that the density increases with the concentration and as the density increases it becomes increasingly difficult to compress a medium. Hence, these variations in  $\chi$  show the existence of strong solvent-solute interactions. At a given concentration, the compressibility decreases with the temperature. It is due to the fact that as the temperature increases, the bond lengths increase and there is greater scope for less compression of the medium.

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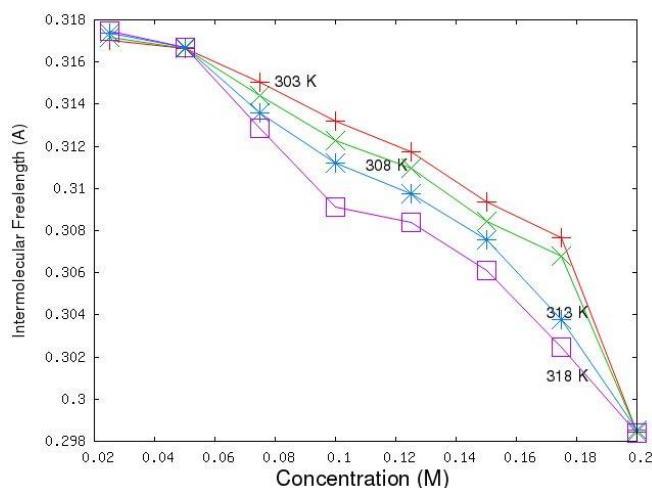


Fig. 7 Calculated Free-length in ValcYTE-Distilled water solution at different concentrations and Temperatures

Figure 7 shows the variation of intermolecular free length of the mixture solution with concentration and temperature. At a given temperature, as the concentration increases,  $L_f$  decreases. It means the average distance between surfaces of neighbouring molecules is getting reduced. This indicates that the attractive forces between the molecules have become strong than in the pure solvent, which indicate strong solute-solvent interactions. At a given concentration, the free length decreases with increase in temperature which is as expected.

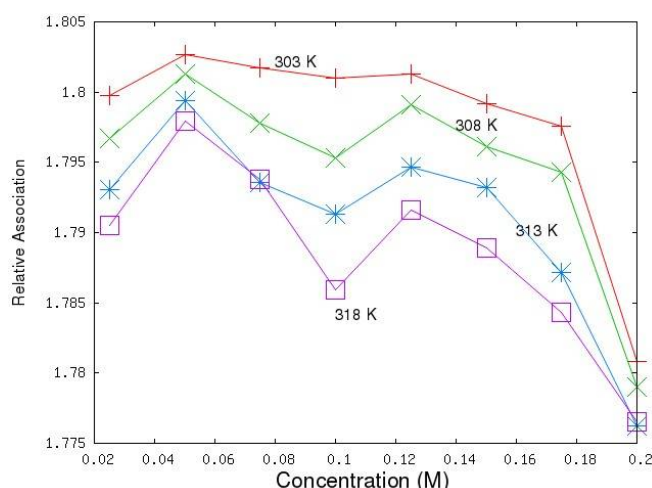


Fig. 8 Calculated Relative Association in ValcYTE-Distilled water solution at different concentrations and Temperatures

Fig. 8 shows the variation of Relative Association (RA) of the mixture solution with concentration and temperature. Relative association slowly decreases with the concentration and the rate of decrease is higher at higher concentrations. at higher concentration. Such decrease in RA indicates weak solute-solvent interaction. Hence, at lower concentrations there is strong solute-solvent interactions and the strength of interaction decreases as the concentration increases. For a given concentration, the RA decreases with increase in temperature, which is due to increase in bond lengths and lattice vibrations at elevated temperatures

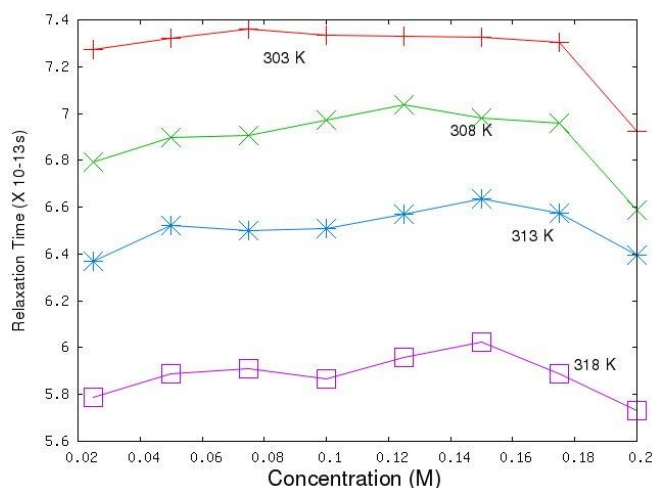


Fig. 9 Calculated Relaxation Time in Valcyte-Distilled water solution at different concentrations and Temperatures

Fig. 9 shows the variation of viscous relaxation time ( $\tau$ ) in the mixture solution with concentration and temperature. As the concentration increases, in general,  $\tau$  increases very slowly. That means, any external excitation energy given to the solution, would take increasingly more time to convert into translational degrees of freedom or translational energy as the concentration increases. This increase in  $\tau$  is due to increase in viscosity of the solution with concentration. At higher temperatures and high concentrations,  $\tau$  decreases marginally. This again follows the viscosity variation trends shown in the fig. 4. At a given concentration, as the temperature is increased,  $\tau$  decreases. This is due to increase in the lattice vibrations at higher temperatures, which would help in easier dissipation of excitation energy into translational energy.

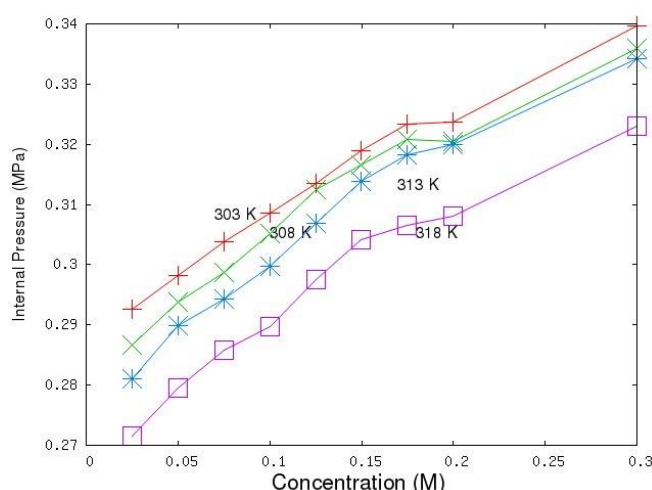


Fig. 10. Calculated Internal Pressure in Valcyte-Distilled water solution at different concentrations and Temperatures

The variation of internal pressure in the Valcyte-Distilled water mixture with concentration and temperature has been shown in the fig. 10. Internal pressure or stress is due to the internal arrangement of the molecules. As the molecular arrangement changes with the concentration, rearrangement of molecules would take place, which would alter the internal stress field or internal pressure. It has been observed from the fig. 10 that as the concentration increases the internal pressure increases almost linearly. This would indicate stronger solute-solvent interactions in the solution. It is

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observed that for a given concentration internal pressure decreases with temperature. Similarly, enthalpy of the mixture solution increases with concentration as shown in the fig. 11.

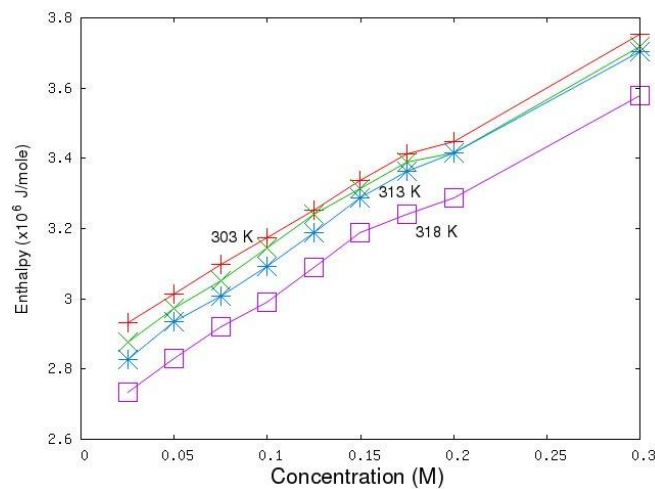


Fig. 11 Calculated Enthalpy in Valcyte-Distilled water solution at different concentrations and Temperatures

Figures 12-15 show variation of molar volume, Vander Waal constant, Rao's constant and Wada constant respectively of the Valcyte-Distilled water solution with concentration and temperature. The trends of variation of these quantities appear almost the same. At all temperatures the variation with concentration is linear resembling that of ideal solution mixture.

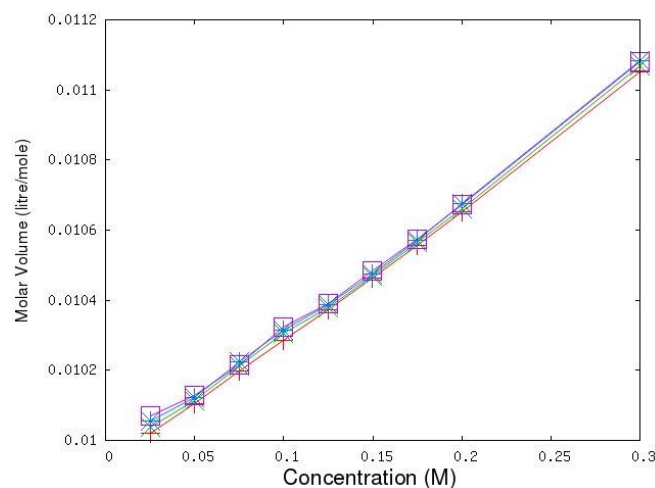


Fig. 12 Calculated Molar Volume of Valcyte-Distilled water solution at different concentrations and Temperatures

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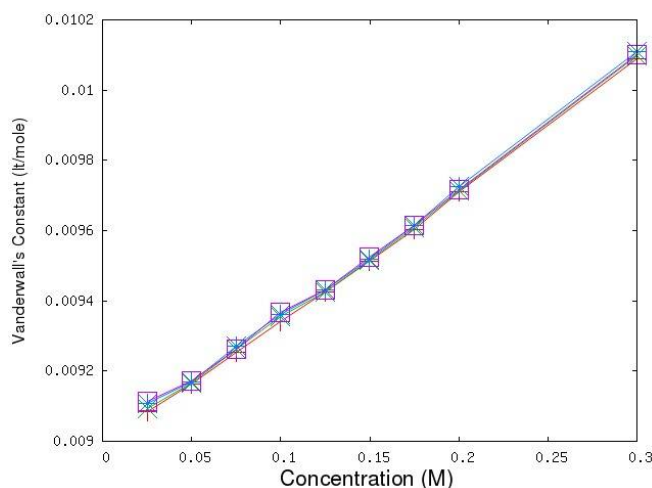


Fig. 13 Calculated van der Waal's Constant of Valcyte-Distilled water solution at different concentrations and Temperatures

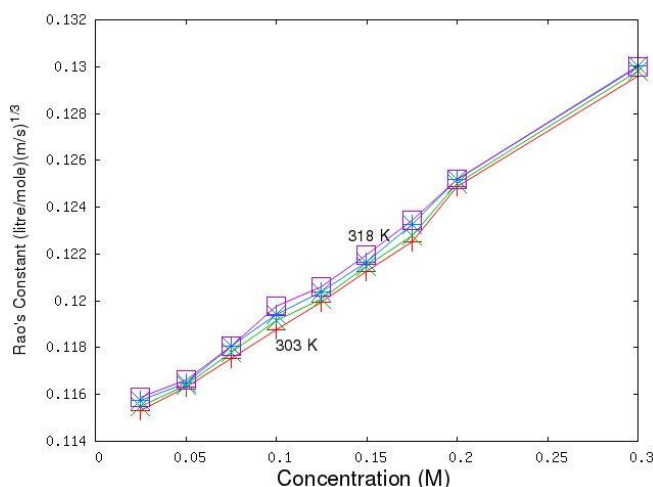


Fig. 14 Calculated Rao's Constant of Valcyte-Distilled water solution at different concentrations and Temperatures

### Nature of Solute-Solvent interaction:

In view of the above results and discussion, it can be concluded that there exists strong solute-solvent interaction. Especially the nonlinear behaviour of molar volume, Rao's constant, etc. strongly indicate this point. The reason for such strong interaction between Valcyte and Water is due to formation of H-bonds between those molecules, which can be explained using their molecular structures.

Hydrogen bonding is a very strong type of dipole-dipole attraction, which is due to electrostatic attraction between two polar groups that occurs when an H atom covalently bound to a highly electronegative atom such as N, O, or F experiences the electrostatic field of another highly electronegative atom nearby. Hydrogen bonds exist between different molecules (intermolecular) of Water.

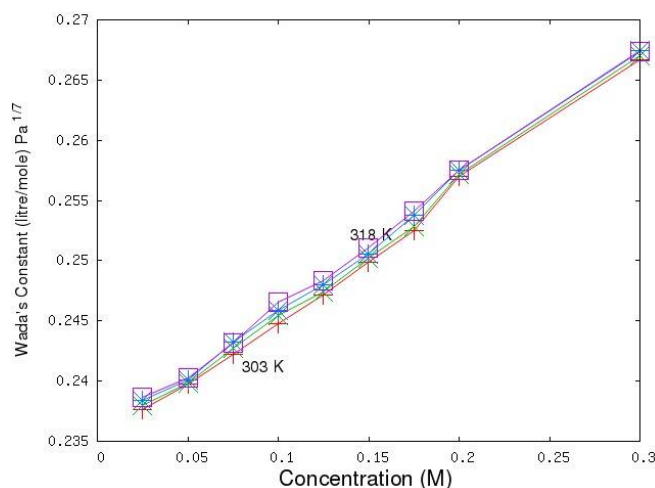


Fig. 15 Calculated Wada's Constant of Valcyte-Distilled water solution at different concentrations and Temperatures

The molecular structure of Valcyte has already been shown in the fig. 1. From reference [15], it can be found out that the Hydrogen Bond Donor Count and Acceptor Count for an Efficient molecule are 5 and 7 respectively. That means, a Valcyte molecule has 5 donor atoms for H bonding with other molecules and 7 acceptor atoms for H bonding from other molecules. Hence, when Valcyte is added to water, strong H-bonds will form between solute and solvent molecules. This is why we see indication of existence of strong solute-solvent interactions in all the figures and results discussed above.

#### IV. CONCLUSION

Molecular Interactions of Valganciclovir-hydrochloride with distilled water have been investigated using experimental and computational techniques. The drug has been added in specific quantities to 99% pure Methanol liquid to obtain certain molarity mixture solutions ranging from 0.025 M to 0.2 M. 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 303 K to 318 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.

#### V. ACKNOWLEDGMENTS

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