



Molecular Interaction Study of Caffeine with Metal Ions in Aqueous Solution through Internal Pressure

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Abstract

Ultrasonic speed (u), density (d) & viscosity (η) of caffeine in aqueous solution of 0.1M, 0.05M, 0.025M potassium chloride, sodium chloride, magnesium chloride & calcium chloride have been measured at 308.15 K. From these Experimental data internal pressure of caffeine in presence of electrolyte solution at infinite dilution are evaluated. These values have been employed to explain molecular association and solute solvent interaction through hydrogen bonding, internal pressure & solvation.

Introduction

Nucleic acids exist in a dynamic equilibrium with a number of molecules that constantly interact with it and regulate cellular activities. The investigation on the study of interaction between xanthine derivatives and metal ions and their molecular behavior¹⁻⁸ shows significant change in the light of molecular interactions. Xanthine derivatives are found to be gain lot of significance in drug delivery systems to specify RNA target. Especially ligand like caffeine can very well interact with the metal RNA structures and capable of altering the conformation of purine structure. The metal RNA binding interaction of methyl xanthine, caffeine, theophylline and theobromine is quite useful to understand the molecular interaction with metal ions when they are target upon a cell and to form the basis for the development of RNA base drugs. The purine constitutes an important class of anti inflammable agents. Important members of this class include theophylline, theobromine and caffeine. It has also been postulated that the purine drugs act by reducing the binding of calcium in the membrane and myoplasm of the cell, thereby the contractility of the muscles. A number of closely related compounds may be regarded as simple methylated derivatives of xanthine or they may be regarded as derivatives of purines. They occur in a number of vegetable products used throughout the world in beverages such as tea, coffee, coca etc. All these beverages causes stimulation of central nervous system but there is no evidence that they are harmful when used in moderation. The xanthines of importance are caffeine, theophylline and theobromine. They are similar in their physiological activity, but there is a considerable difference in the intensity of action on various structures. Literature survey indicates that the scanty data is available on caffeine in aqueous solution of electrolyte. Hence it was thought of interesting to study the volumetric,



viscometric and acoustical behavior of caffeine in presence of Na^+ , K^+ , Ca^{2+} and Mg^{2+} ions through internal pressure.

Experimental

Caffeine (Kores India Ltd. Pharmaceuticals and Chemical Division, 99.5% pure) was used after drying for 24 hours. Salts of NaCl , KCl , CaCl_2 , MgCl_2 , ZnCl_2 , CuCl_2 (Sd-fine chemical, 99.5% pure) were used as such without further purification except drying over P_2O_5 in a desiccators for 2 days. Doubly distilled demonized and degassed water having conductance $0.6 \times 10^{-6} \text{ Scm}^{-1}$ was used during the course of entire work. All the solutions kept in a airtight bottles. The weighing was done on Shimadzu Ax-120 electronic balance precisely up to $1 \times 10^{-4} \text{ g}$. All the solutions were prepared just before their use. Density measurements were precise much better than $5 \times 10^{-2} \text{ kgm}^{-3}$. Ultrasonic velocity was measured with a variable path ultrasonic interferometer at 2 MHz. The repeatability of velocity measurement was $\pm 0.1 \text{ ms}^{-1}$. Viscosity measurements were performed with pre-calibrated Ostwald type viscometer. The percentage error in the determination of viscosity was $\pm 0.02\%$. The accuracy in the Experimental temperature was maintained at $(\pm 0.01 \text{ K})$ by means of thermostatic bath.

Results & Discussion

In case liquids, it is well known that the attractive forces between two non-polar molecules vary inversely as the seventh power of their molecular magnitude, when the intermolecular distance are of the order of little more than the molecular diameter. Thus the powerful cohesive forces are responsible for the main properties of liquid state. In the interior of liquids there is a balance between the attractive and repulsive forces that produces internal pressure (P_i), which is found to be an important parameter for explaining the various characteristics of liquid and liquid mixtures and to study different types of chemical reactions initiated by sound velocity¹.

Internal pressure has been found to be a very important parameter in the theory of liquid state². It reflects the sum of total balance of solute-solvent, solute-solute and solvent-solvent interactions in a liquid state of solution. The study of internal pressure was initiated by Hidebrand and Scott⁽³⁻⁴⁾ and later on reviewed by many workers⁵ to show the significance of internal pressure as a fundamental property of liquid state and co-relation with other properties for binary liquid mixtures, internal pressure has been used to investigate the molecular interactions.⁶⁻⁷ In 1925, the first review of the internal pressure was given by Richards⁸. In the broader sense, Internal pressure is a measure of the totality of forces of attraction, repulsion ionic and dipolar interactions that contribute to the overall cohesion of liquid system including electrolytes and non-electrolytes.

Barton⁹ discussed the relation between internal pressure and cohesive energy density values. Several workers have studied the importance of internal pressure in understanding the nature of liquids and solution. Macdonald¹⁰ et al have reported internal pressure and cohesive energy density of liquid



mixtures. Staveley¹¹ et al predicted interactions in the liquid mixtures by comparing the internal pressure of individual liquid components and its variation with concentration and temperature. Collins¹² et al derived an equation for evaluation of P_i and predicted that the P_i values of many pure molecular liquid using ultrasonic and thermodynamic data.

Dhanlaxmi¹³ has reported that the viscosity and internal pressure of mixtures as well as that of pure solvents at a given temperature fall exponentially with increase in content of non-polar solvent. Pandey and Chaturvedi¹⁴ have successfully evaluated the internal pressure values in the case of many liquid metals using their relations. Singh¹⁵ et al have reported the cause of non-idealities in properties of solutions or liquid mixtures and suggested that the nature and the extent of interaction among the molecular species present in the liquid mixtures are responsible for such idealities. Moor¹⁶ has studied the internal pressure of diethyl ether Patterson¹⁷ et al have discussed at length the importance of internal pressure in liquids and liquid mixtures. Dubey and co-workers¹⁸ have used the internal pressure to study the molecular interactions in binary liquid mixtures Suryanarayana¹⁹ has reported the effect of temperature on the internal pressure and observed that fall of internal pressure with temperature either for pure liquids or for homogenous solutions.

During recent years, attempts have been made to determine the internal pressure of liquid mixture. Extensive work has been carried out excess thermodynamic properties like excess internal pressure²⁰⁻²³, which are used to study intermolecular interactions in binary liquid mixtures. Pandey and Gupta evaluated excess internal pressure in binary ionic liquid mixtures.

The internal pressure, thermodynamically of a liquid is given by

$$(\partial U / \partial V)_T = P_{\text{int}} = T (\partial P / \partial T)_V - P \quad 1$$

$$\text{i.e. } P_{\text{int}} = [(\alpha T / \beta_T) - P] \quad 2$$

where P is the external pressure. β, α is coefficient of thermal expansion β_T is isothermal compressibility and T is temperature zero pressure the above equation reduces to

$$P_{\text{int}} = [(\alpha T / \beta_T) \beta] \quad 3$$

Suryanarayana and Kuppaswami obtain a relation, which relates the free volume to the sound velocity u and viscosity η by the following expression.

$$V_f = [(Mu / K\eta)^{3/2}] \quad 4$$

where M is the molecular weight of liquid K is a dimensionless constant independent of temperature and nature of liquid having a value 4.28×10^9 in CGS unit. Using free volume concept, on the basis of dimensional analysis, the expression for internal pressure is given by

$$P_{\text{int}} = bRT [(K\eta / u)^{1/2} (d^{2/3} / M_{\text{eff}}^{7/6})] \quad 5$$

where b is packing factor having the value 2 and d is density of liquid mixture.



From the above equation one can compute the internal pressure of liquid system directly from the Experimental values of velocity and density.

Table: 1 Internal pressure of caffeine in aqueous solution of sodium chloride and potassium chloride at 308.15 K.

Conc.of sodium chloride	Conc. of caffeine m	Internal pressure $P_i \times 10^5$ (Pa)	Conc. of potassium chloride	Conc. of caffeine m	Internal pressure $P_i \times 10^5$ (Pa)
0.1 M	0.0100	81438.40	0.1 M	0.0100	65839.82
	0.0200	68967.19		0.0200	58123.94
	0.0300	61055.79		0.0300	52932.05
	0.0401	55596.59		0.0401	49187.62
	0.0502	51613.91		0.0501	46339.57
	0.0603	48581.44		0.0603	44139.04
	0.0705	46244.25		0.0704	42378.20
	0.0807	44330.02		0.0807	40939.98
	0.0909	42751.11		0.0909	39733.40
0.05 M	0.0100	81520.08	0.05 M	0.0100	65804.38
	0.0200	69004.12		0.0200	58123.98
	0.0300	61064.44		0.0300	52907.50
	0.0401	55586.04		0.0401	49147.90
	0.0503	51583.60		0.0502	46312.88
	0.0604	48535.52		0.0603	44105.42
	0.0707	46146.18		0.0705	42325.36
	0.0809	44214.83		0.0808	40874.53
	0.0912	42628.62		0.0910	39668.37
0.025 M	0.0100	77219.00	0.025 M	0.0099	65846.67
	0.0200	69086.23		0.0200	58133.67
	0.0301	61130.41		0.0301	52917.12
	0.0402	55636.05		0.0402	49158.07
	0.0503	51617.63		0.0503	46313.05
	0.0605	48561.17		0.0605	44069.68
	0.0707	46146.32		0.0707	42293.82
	0.0809	44211.96		0.0810	40841.89
	0.0912	42599.67		0.0912	39628.76



Table: 2 Internal pressure of caffeine in aqueous solution of calcium chloride and magnesium chloride at 308.15 K.

Conc. of calcium chloride	Conc. of caffeine m	Internal pressure $P_i \times 10^5$ (Pa)	Conc. of magnesium chloride	Conc. of caffeine m	Internal pressure $P_i \times 10^5$ (Pa)
0.1 M	0.0100	34215.76	0.1 M	0.0099	24539.66
	0.0200	33268.21		0.0198	24665.92
	0.0300	32535.79		0.0298	24790.99
	0.0401	31941.04		0.0398	24899.38
	0.0501	31454.30		0.0498	25000.62
	0.0603	31048.52		0.0600	25089.70
	0.0704	30707.13		0.0700	25174.56
	0.0807	30418.39		0.0801	25258.03
	0.0909	30173.08		0.0903	25334.53
0.05 M	0.0100	34215.19	0.05 M	0.0099	24526.14
	0.0200	33267.88		0.0200	24647.52
	0.0300	32513.44		0.0300	24764.95
	0.0401	31904.84		0.0400	24868.54
	0.0502	31404.61		0.0500	24966.18
	0.0603	30992.19		0.0600	25058.64
	0.0705	30639.20		0.0701	25137.52
	0.0808	30334.69		0.0803	25210.91
	0.0910	30071.77		0.0905	25282.63
0.025 M	0.0099	34213.28	0.025 M	0.0100	24484.79
	0.0200	33246.78		0.0200	24614.62
	0.0301	32478.86		0.0300	24720.77
	0.0402	31855.77		0.0401	24813.03
	0.0503	31346.01		0.0502	24893.53
	0.0605	30917.68		0.0603	24970.50
	0.0707	30555.57		0.0705	25043.70
	0.0810	30242.04		0.0807	25105.21
	0.0912	29973.66		0.0909	25163.76



The experimentally calculated values of internal pressure for caffeine in 0.1M, 0.05M and 0.025M aqueous solution of sodium chloride, potassium chloride calcium chloride and magnesium chloride are tabulated in Table 1&2. The internal pressure values are found to decrease with the increase in concentration of caffeine in all solution of sodium chloride, potassium chloride calcium chloride and magnesium chloride. The P_i values in case of caffeine sodium chloride systems for 0.1M concentrations are higher as compared to 0.05M and 0.025M.

A similar trend of P_i values is observed in case of caffeine + KCl, caffeine + CaCl_2 and caffeine + MgCl_2 systems. It is observed from data of Table 1&2. that the values of P_i for caffeine in monovalent metal ions such as Na^+ and K^+ are higher as compared to P_i values for divalent metals Ca^{2+} and Mg^{2+} . The values of P_i are higher for Na^+ as compared to caffeine in K^+ ions. Similar trend of higher values of P_i for Ca^{2+} as compared to caffeine Mg^{2+} is observed. The order of P_i values of caffeine in metal ions is $\text{NaCl} > \text{KCl} > \text{CaCl}_2 > \text{MgCl}_2$.

Conclusion

The studied Experimental techniques like volumetric, ultrasonic, and viscometric play a significant role in exploring the nature and interactions of biomolecules with metal ions. The derived parameters also help to assess the molecular interactions in biological system. The metal ions have strong complexing tendency with xanthine-based compounds. This fact cannot be only explained on the basis of solute-solvent interactions or electrostriction by assessing all the study parameters. Such interaction study on simple model system produces better understanding of the nature of solute-solvent interactions, thereby providing insight into the role of solvent in stabilizing/ destabilizing biologically important molecules. Further detail investigation and study is requiring shedding some light on the interactions amongst the biomolecules and the metal ions.

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