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RESEARCH ARTICLE

Acoustical Studies on Heterocyclic Drugs In 1,4- Dioxane at 303.15 K

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Abstract

Objective: Main objective is to study the solute solvent interactions in different heterocyclic drugs with the help of various acoustic properties. **Method:** The values of ultrasonic velocity are measured by using ultrasonic interferometer for solution of different concentrations of heterocyclic drugs (Lamivudine, Simvastatin) in 70% 1,4-dioxane as a solvent at 303.15 K. This experimental data is used to explore the acoustic properties like as intermolecular free length (L_f), adiabatic compressibility (β_s), apparent molal volume (ϕ_v), specific acoustic impedance (Z), apparent molal compressibility (ϕ_k), limiting apparent molal compressibility (ϕ_k^0), limiting apparent molal volume (ϕ_v^0), relative association (R_A), solvation number (S_n) with respect to change in concentration. **Finding :** It is noticed that the solute solvent interaction between the heterocyclic drugs and dioxane systems are strong. **Novelty:** Heterocyclic drugs viz. Lamivudine and Simvastatin were used to study different acoustic properties. In present work the acoustic properties of Lamivudine and Simvastatin in 1,4-dioxane at 303.15K have been reported.

Keywords: Lamivudine, Simvastatin, intermolecular free length, apparent molal volume, adiabatic compressibility, ultrasonic velocity.

1 Introduction

In the modern research, interpretation of solute-solvent, ion-solvent interaction in non-aqueous and aqueous medium is done via measurements of the Ultrasonic velocity[(1)]. Ultrasonic studies may throw more light on the molecular interaction to know the behavior of solute and solvent molecules in liquid mixtures and solutions[(2)]. The acoustical properties of different drugs in methanol have been determined and the conclusion was drawn from adiabatic compressibility that the solvent methanol compress by four different drugs to the same extent but their solute-solvent interaction is different due to the difference in their size, shape and structure[(3,4)]. The different acoustical properties of some substituted Pyrazolines in acetone-water binary mixture have been determined[(5)] and it is observed that the ultrasonic velocity vary with concentration. The ultrasonic velocity and density of amino acid in aqueous solution of magnesium acetate at constant temperature have been investigated[(6)], which indicates the ion-dipole interaction largely influenced by the size of ion and polarity of solvent.

The strength of ion-dipole attraction is directly related to the ion size and magnitude of dipole but inversely related to the space between molecules and ion.

Acoustical properties of polymer solutions have shown that ultrasonic velocity and its derived parameters provide much information on molecular interactions, which are of utmost importance for processes involving polymer production and their uses[7,8]. The thermodynamic and acoustical properties of citric acid in water at various temperatures have been studied, the nature of variation of acoustic parameters with concentration and temperature has been used to understand the type and strength of interaction present in the system[9]. The ultrasonic velocity and density in solutions of new Schiff bases and their metal complexes of Co (II), Ni (II) and Cu (II) have been measured and various acoustical parameters have been calculated in non-aqueous medium[10]. The thermodynamic parameters and acoustic properties for the solution of amide and amines in benzene were also studied to calculate the thermo dynamical parameters which helped to find the existence of strong molecular association. Such a molecular association is found to be by hydrogen bonding and through dipole-dipole interaction[11]. It is observed that there has not been much research carried out in the measurements of density and ultrasonic velocity of narcotic analgesic drugs for understanding their physico-chemical behaviour in terms of drug-solvent interactions in aqueous-alcoholic systems, the different acoustical parameters of water and 1-propanol binary mixture have been studied[12]. The existence of ion-solvent or solvent-solvent interaction resulting in attractive forces promote the structure-making tendency, while ion-ion or solute-solute interaction resulting dipole-dipole, dipole induced dipole and electrostrictive forces enhance the structure-breaking properties[13]. Whereas, the molecular interactions in liquid have been studied from density, viscosity, sound velocity and conductance measurements[14].The survey of literature shows that, the detail study of above-mentioned drugs under indistinguishable set of experimental circumstance is still lacking. It was thought of interest to study the acoustical properties of said drugs under appropriate condition.

2 Materials and methods

In the present study, the drug Lamivudine and Simvastatin was used. The solution of different concentration of drug was prepared in 1,4- dioxane (AR grade,99.8% pure). The specific gravity bottle used to determine the densities by relative measurement method. The ultrasonic velocity was measure by using ultrasonic interferometer having frequency 3 MHz (Mittal Enterprises, Model No. F-81). The constant temperature was maintained by circulating water through the double wall measuring steel cell. In the present analysis, different properties such as intermolecular free length, adiabatic compressibility, apparent molal volume, apparent molal compressibility, relative association, specific acoustic impedance, limiting apparent molal compressibility, limiting apparent molal volume, solvation number and their constant have been evaluated.

2.1 Theoretical Calculations

Adiabatic compressibility βs is given by:

$$\beta s = \frac{1}{Us^2\, ds} \tag{1}$$

Where, U_s is ultrasonic velocity of solution.

Apparent molal compressibility (ϕ_k) has been calculated by using the relation

$$(\phi_k) = 1000 * \left(\frac{\beta s\, d_{0-}\, \beta_0 d_s}{m * d_s * d_0} \right] + \frac{\beta_s * M}{d_s} \tag{2}$$

Where,$\beta_s, d_0$and β_0,$d_s$are the adiabatic compressibility and density of solution and solvent respectively. m is molal concentration of solute, M is molecular weight of solute.

Apparent molal volume ϕ_v

$$(\phi_v) = \frac{M}{d_s} * \frac{(d_0 - d_s) * 10^3}{m * d_s * d_0} \tag{3}$$

Specific acoustic impedance

$$(Z) = U_S * ds \tag{4}$$

Intermolecular free length

$$\left(L_f\right) = K\sqrt{\beta}_s \tag{5}$$

Where, K is the temperature dependent Jacobson's constant is calculated by using relation

$$K = (93.875 + 0.375 * T) * 10^{-8} \tag{6}$$

Where, T is temperature at which experiment is carried out.

$$(R_A) = \left(\frac{d_S}{d_0}\right) * \left(\frac{U_0}{U_S}\right)^{\frac{1}{3}} \tag{7}$$

$$\phi_k = \phi_k^0 + S_k C \tag{8}$$

$$\phi_v = \phi_v^0 + S_v C \tag{9}$$

3 Results and Discussion

In the present investigation, different acoustical properties like adiabatic compressibility(β_s), specific acoustic impedance $(Z)$and intermolecular free length $\left(L_f\right)$(Table1), solvation number (S_n), relative association(R_A), apparent molar volume (ϕ_v), apparent molar compressibility(ϕ_k) (Table2), limiting apparent molal compressibility$\left(\phi_k^0\right)$, limiting apparent molal volume$\left(\phi_v^0\right)$ and their constant $\left(S_{k,}\ S_v\right)$ (Table3) are determined from the ultrasonic velocity and density measurements of the solution.

Table 1. Acoustical parameters for Lamivudineand Simvastatin at different concentrations

Concentration $C * 10^{-3}$	Density (d_s)	Ultrasonic velocity (U_s)	Adiabatic compressibiliy $\beta_s * 10^{-10}$	Intermolecular free length $L_f * 10^{-11}$	Specific acoustic impedance $Z * 10^6$
moles lit^{-1}	kg m-^{3}	m s^{-1}	m^{2}N^{-1}	m	kg m^{-2} s^{-1}
			Lamivudine + 1,4-Dioxane		
1.0	1019.75	1495.20	4.3864	4.2122	1.5247
2.0	1019.89	1501.26	4.3505	4.1949	1.5311
3.0	1020.01	1512.72	4.2843	4.1629	1.5430
4.0	1020.13	1519.26	4.2470	4.1447	1.5498
5.0	1020.22	1526.52	4.2063	4.1248	1.5574
6.0	1020.29	1532.46	4.1735	4.1087	1.5636
7.0	1020.36	1537.38	4.1465	4.0954	1.5687
8.0	1020.40	1545.12	4.1049	4.0748	1.5766
9.0	1020.46	1552.86	4.0639	4.0544	1.5846
			Simvastatin + 1,4-Dioxane		
1.0	1019.91	1489.86	4.4172	4.2270	1.5195
2.0	1020.07	1495.50	4.3833	4.2107	1.5255
3.0	1020.24	1503.06	4.3386	4.1892	1.5335
4.0	1020.35	1506.36	4.3191	4.1798	1.5370
5.0	1020.47	1512.78	4.2820	4.1618	1.5437
6.0	1020.57	1517.16	4.2569	4.1496	1.5484
7.0	1020.66	1525.26	4.2114	4.1274	1.5568
8.0	1020.75	1529.04	4.1903	4.1170	1.5608
9.0	1020.81	1536.06	4.1518	4.0980	1.5680

The results indicate that ultrasonic velocity and density of heterocyclic drugs increase with increasing concentration. (Table 1). Variation of ultrasonic velocity in solution depends upon the increase or decrease of molecular free length after mixing the component. This is based on a model for sound propagation proposed by Eyring and Kincaid [15]. Intermolecular free length decreases with increasing concentration of solution due to greater force of attraction between solvent and solute molecule by

Table 2. Concentration, Relative association, Apparent molal compressibility, Apparent molal volume, Solvation number of Lamivudine and Simvastatin.

Concentration $C * 10^{-3}$	Apparent molal volume (ϕ_v)	Apparent molar compressibility $\phi_k * 10^{-10}$	Relative association (R_A)	Solvation number (S_n)
moles lit^{-1}	$m^3 mole^{-1}$	$m^2 N^{-1}$		
		Lamivudine + 1,4-Dioxane		
1.0	0.0325	0.9859	0.9990	0.9882
2.0	0.0613	0.9775	0.9971	0.9798
3.0	0.0773	0.9622	0.9947	0.9645
4.0	0.0853	0.9536	0.9934	0.9558
5.0	0.0959	0.9442	0.9919	0.9464
6.0	0.1061	0.9366	0.9907	0.9388
7.0	0.1135	0.9304	0.9897	0.9325
8.0	0.1225	0.9208	0.9881	0.9229
9.0	0.1275	0.9113	0.9865	0.9135
		Simvastatin + 1,4-Dioxane		
1.0	0.0642	1.8128	1.0005	0.9952
2.0	0.1603	1.7985	0.9986	0.9873
3.0	0.1892	1.7797	0.9971	0.9770
4.0	0.2180	1.7715	0.9964	0.9725
5.0	0.2333	1.7560	0.9951	0.9640
6.0	0.2468	1.7455	0.9943	0.9582
7.0	0.2577	1.7266	0.9926	0.9478
8.0	0.2659	1.7177	0.9919	0.9430
9.0	0.2755	1.7017	0.9904	0.9342

Table 3. Limiting Apparent molal compressibility (ϕ_k^0), Limiting Apparent molal volume (ϕ_v^0), S_v and S_k of Lamivudine and Simvastatin.

Drugs	Limiting Apparent molal volume (ϕ_v^0)	Limiting Apparent molal compressibility $(\phi_k^0) * 10^{-9}$	S_v	S_k
	$m^3 mole^{-1}$	$m^2 N^{-1}$	$m^3 kg^{1/2} mole^{-3/2}$	$m^3 mole^{-2}$ kg N^{-1}
Lamivudine	0.0366	0.9927	10.949	-9.1507
Simvastatin	0.1017	1.8294	22.133	-13.6500

creating hydrogen bonding. It was occurred due to strong interaction between solvent and ion molecules suggesting a structure-promoting behavior of the added electrolyte. The specific acoustic impedance increases with the increasing concentration of the solution. This indicates a strong intermolecular interaction between solute and solvent molecules in the system at higher concentration and suggests more association between solute and solvent molecules in the system [16]. It was observed that apparent molal volume increased with concentration, indicates the existence of strong solute-solvent interaction. The adiabatic compressibility decreases with the increase in concentration of solution. It shows weak electrostatic force of attraction between the close vicinity of ions. From the data, it has been concluded that there are weak molecular association was found in both drugs. The value of relative association is decreases with increasing the concentration of solution. It has been observed that there was weak solute-solvent interaction. Relative association is an acoustic property of understanding interaction, which is influenced [17,18] by two opposing factors:

1. The breaking up of solvent molecules on addition of solute to it and
2. Solvation of the solute molecule

The former leads to decrease and the latter to the increase of relative association. In our study the values of relative association decrease with increase in the solute concentration due to breaking up of solvent molecules.

There was a decrease in solvation number as the concentration of solution increases; it indicates the strong coordination bond forms by solvent molecule in primary layer and due to this decrease in size of secondary layer of solvation are observed. The value of S_k exhibits negative. It indicates the presence of weak solute-solute or ion-ion interactions in the given heterocyclic drugs. From Table3, it was observed that the value of limiting apparent molal volume is positive for both drugs. It indicates that the ion-dipolar interaction in Lamivudine, Simvastatin and 1, 4 dioxane. The all value of S_v are positive, indicates the strong interaction between solvent and solute molecule. These values indicate an induced effect of 1, 4 dioxane on solvent-solute interaction. From Figures 1 and 2 the value of S_k and S_v has been determine. Similar studies were performed with different heterocyclic drugs viz. Acarbose, Haloperidol, Etodolac, Thiabendazole, Digoxin in 1,4-dioxane[19–21] wherein similar results were found regarding molecular interactions with the above-mentioned heterocyclic drugs.

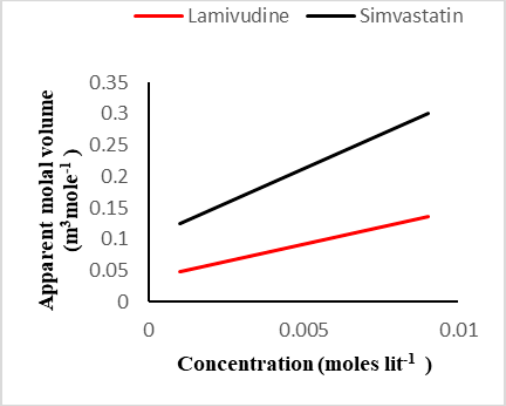

Fig 1. Apparent molal volume (m^3mole^{-1}) Vs Concentration (mole lit^{-1})

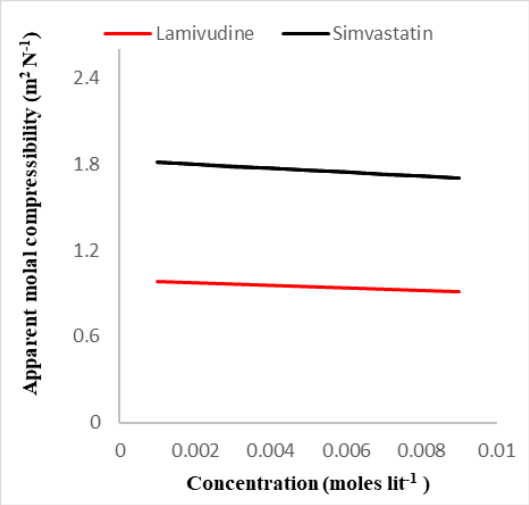

Fig 2. Apparent molal compressibility ($m^2\ N^{-1}$) Vs Concentration (mole lit^{-1})

4 Conclusion

The present study describes the acoustic properties that confirm the molecular interaction of heterocyclic drugs (Lamivudine, Simvastatin) with dioxane. The acoustic parameters like adiabatic compressibility, intermolecular free path length, acoustic impedance, relative association, apparent molal volume, apparent molal compressibility, solvation number and relaxation time have been estimated using experimental data. The variations in the acoustic parameters suggest that there are strong solute-solvent interactions at higher concentration.

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