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Thermodynamics studies of an Atorvastatin Drug in aqueous medium at different temperatures and concentrations

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ABSTRACT:

In the present study ultrasonic velocity (υ), density (ρ) and viscosity (η) have been measured at frequency 2 MHz in the binary mixtures of Atorvastatin with water in the concentration range (0.1 to 0.0125 %) at 303 K,308 K, 313 K using Multifrequency ultrasonic interferometer . The measured value of density, ultrasonic velocity, and viscosity have been used the acoustical parameters namely adiabatic compressibility (κ), relaxation time (τ), acoustic impedance (z), free length (L_f), free volume (V_f) and internal pressure (Πi), Wada's constant (W), Rao's Constant(R), cohesive energy (CE) were calculated. The obtained results support the complex formation, molecular association by intermolecular hydrogen bonding in the binary liquid mixtures.

Key Words: Atorvastatin, ultrasonic velocity, acoustical parameters.

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INTRODUCTION:

Atorvastatin is a member of the drug class known as statins, used for lowering blood cholesterol. Chemically, it is (3R, 5R)-7-(2-(4-flurophenyl)-3-phenyl-4(phenylcarbinol l)-5-propan-2-3,5dihydroxyheptanoicacid. Like all statins, Atorvastatin works by inhibiting HMG-CoA reductase, an enzyme found in liver tissue that plays a key role in production of cholesterol in the body. The primary uses of Atorvastatin are for the treatment of dyslipidemia and the prevention of cardiovascular disease. It is recommended to be used only after other measures such as diet, exercise, and weight reduction have not improved cholesterol levels [1].

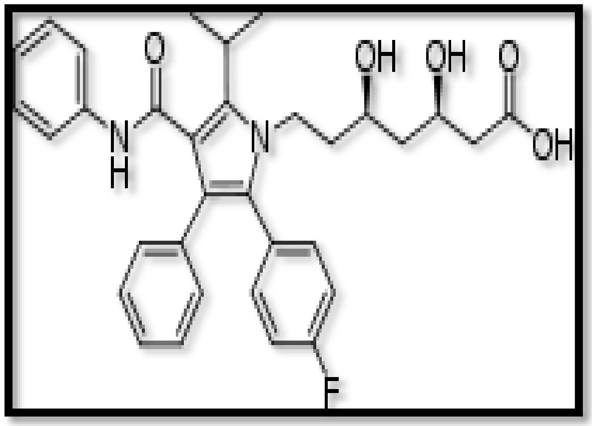

Figure: chemical structure of Atorvastatin

Ultrasonic waves are used in many applications including plastic welding, medicine, jewelry cleaning, pipe inspection, and nondestructive test. Within nondestructive test, ultrasonic waves give us the ability to 'see through' solid / opaque material and detect surface or internal flaws without affecting the material in an adverse manner. It had been identified, about 200 years ago, that dogs could hear [2]. This Canine ability is often used in police department work and by dog trainers. These sound waves are used by bats as kind of navigational radar for night flying [3].Even blind people unconsciously develop a similar method by which obstacles are sensed by the reflected echoes of their footsteps or the tapping of a cane. In the field of technology, the waves are being used to measure depth of sea, directional signaling in submarine, and mechanical cleaning of surface soldering [4], and to detect shoals of fish. Acoustic sonograms have become an important medicinal diagnostic tool which is widely used nowadays [5-6]. Ultrasonic waves are used for both diagnosis and therapy. It includes the detection of wide variety of anomalies, such as tumor, bloodless surgery, proper extraction of broken teeth, cardiology, and stone fragmentation [7]. Ultrasound is more sensitive than X-rays in distinguishing various kinds of tissues. It is believed to be less hazardous than X-rays, although possible hazards of ultrasound have not yet been thoroughly explored [8]. The unique feature of sound wave property is that it gives direct and precise information of the adiabatic properties of solution. The data of velocity of sound in very few liquids were available up to 1930. The discovery of interferometer and optical diffraction method improved the investigation, both qualitatively and quantitatively. Most of the information extracted from ultrasonic study of fluids is confined to the determination of hydration number and compressibility [9-10]. The successful application of acoustic methods to physicochemical investigations of solution becomes possible after the development of adequate theoretical approaches and methods for precise ultrasound velocity measurements in small volumes of liquids [11-13]. In the present paper, viscometric ultrasonic studies have been studied in Water at different temperatures over a wide range of Atorvastatin concentrations. From the experimental values a number of thermodynamic parameters namely ultrasonic velocity, adiabatic compressibility, acoustic impedance, relaxation time, free length, free volume, internal pressure, Rao's constant, ultrasonic attenuation, cohesive energy, and molar volume, Wada's constant has been calculated. The variation of these parameters with concentration was found to be useful in understanding the nature of interactions between the components [14-17].

MATERIALS AND METHODS:

Atorvastatin used in the present work was of analytical reagent (AR) grade with a minimum assay of 99.9%, It is used without purification. Different concentrations of solution were prepared by adding sufficient amount of solvent ethanol to Atorvastatin. The ultrasonic velocity (υ) has been measured in ultrasonic interferometer Mittal Model-F-05 with an accuracy of 0.1%. The viscosities (η) of binary mixtures were determined using Ostwald's viscometer by calibrating with double distilled water with an accuracy of ±0.001 Pa Sec. The density (ρ) of this binary solution was measured accurately. using 25 ml specific gravity bottle in an electronic balance precisely and accurately the basic parameter U, η, ρ were measured at various concentration (0.0125 to 0.1%) and temperature of 303 K,308 K & 313 K. The various viscometric ultrasonic parameters were calculated from υ, η & ρ value using standard formulae. On using ultrasonic velocity, density and viscosity the following acoustical parameters like adiabatic compressibility (κ), intermolecular free length (L_f) , relaxation time (τ) , free volume (V_f) , internal pressure (Π_i) , acoustic impedance (Z) , ultrasonic attenuation (α/f^2) , Rao's constant (R) , molar volume (Vm),cohesive energy (CE) were calculated.[18-26]

Table 1:- Ultrasonic velocity, Density, Viscosity, Adiabatic compressibility, Intermolecular free length, Free volume , Rao's constant of different % concentration of solution of compounds in ethanol at ,303 K, 308 K, 313 K.

a) Solution of Atorvastatin in ethanol at **303 K**.

Concentration (%)	Density (Kgm^{-3})	Viscosity $x10^{-3}$ (Nsm^{-2})	Ultrasonic Velocity (m/s)	Adiabatic compressibility $x10^{-11}$ (m^2 /N)	Intermolecular free length x10^{-11} (m)	Free Volume x10^{-3} (m^3 mol^{-1})	Rao' s constant
0.0125	987.64	0.7363	1490	4.542	4.2118	22.682	1.9578
0.025	989.92	0.7656	1496	4.507	4.2286	21.476	1.9550
0.05	991.96	0.8966	1506	4.438	4.1802	17.116	1.9553
0.1	1013.56	0.9728	1520	4.265	4.0974	15.356	1.9195

b) Solution of Atorvastatin in ethanol at **308 K**.

Concentration (%)	Density (Kgm^{-3})	Viscosity $x10^{3}$ (Nsm^{-2})	Ultrasonic Velocity (m/s)	Adiabatic compressibility x10^{-10} (m^2 /N)	Intermolecular free length x 10^{-11}(m)	Free Volume x10^{-2} (m^3 mol^{-1})	Rao' s constant
0.0125	982.64	0.7403	1472	4.6889	4.3337	22.045	1.9583
0.025	983.88	0.7506	1490	4.5781	4.2821	21.971	1.9639
0.05	988.4	0.8304	1500	4.4786	4.2354	19.129	1.9606
0.1	988.92	0.9454	1510	4.4260	4.2118	15.872	1.9631

c) Solution of Atorvastatin in ethanol at **313 K**.

Concentration (%)	Density (Kgm^{-3})	Viscosity $x10^3$ (Nsm^{-2})	Ultrasonic Velocity (m/s)	Adiabatic compressibility $x10^{-10}$ (m^2/N)	Intermolecular free length $x10^{-11}$(m)	Free Volume $x10^{-2}$ ($m^3 mol^{-1}$)	Rao' s constant
0.0125	979.92	0.6625	1466	4.7354	4.3926	25.911	1.9621
0.025	980.88	0.6808	1470	4.6859	4.3696	25.050	1.9633
0.05	984.88	0.7377	1481	4.4229	4.3402	22.365	1.9584
0.1	986.80	0.8444	1492	4.5495	4.3056	18.468	1.9609

Table 2- Internal pressure, Acoustic Impedance, Relaxation time, Ultrasonic attenuation, Cohesive energy and Molar volume, Wada's constant, at 303 K, 308 K, 313 K

a) Solution of Atorvastatin in ethanol at **303 K**.

Concentration(%)	Internal pressure (Nm^{-2})	Acoustic Impedance ($Kg^{-1} m^2 S^{-1}$)	Relaxation time $x10^{-12}$ (S)	Ultrasonic attenuation $x10^{-10}$ (s^2m^{-1})	Wada' s constant	Cohesive energy (KJ/Mole)	Molar volume (m^3/mol)
0.0125	57.705	1.474546	4.4594	5.8899	3.7018	9.8847	171.29
0.025	58.856	1.481910	4.6020	6.0620	3.69741	10.0588	170.90
0.05	63.568	1.494883	5.3071	6.9444	3.69792	10.8416	170.55
0.1	66.862	1.541624	5.5321	5.5321	3.63987	11.1657	166.99

b) Solution of Atorvastatin in ethanol at **308 K**.

Concentration(%)	Internal pressure (Nm^{-2})	Acoustic Impedance ($Kg^{-1}m^2S^{-1}$)	Relaxation time $x10^{-12}$ (S)	Ultrasonic attenuation $x10^{-10}$ (s^2m^{-1})	Wada' s constant	Cohesive energy (KJ/Mole)	Molar volume (m^3/mol)
0.0125	59.0283	1.4478	4.6288	6.1966	3.7028	10.1599	172.1198
0.025	59.1676	1.4659	4.5817	6.0636	3.7118	10.1739	170.9518
0.05	62.1171	1.4855	4.9588	6.5059	3.7065	10.6323	171.1655
0.1	66.1277	1.4942	5.5832	7.2863	3.7104	11.3128	171.0755

c) Solution of Atorvastatin in ethanol at **313 K**.

Concentration(%)	**Internal pressure (Nm^{-2})**	**Acoustic Impedance ($Kg^{-1}m^2S^{-1}$)**	**Relaxation time $x10^{-12}$ (S)**	**Ultrasonic attenuation $x10^{-10}$ (s^2m^{-1})**	**Wada' s constant**	**Cohesive energy (KJ/Mole)**	**Molar volume (m^3/mol)**
0.0125	56.7257	1.4385	4.1830	5.6189	3.7089	9.7935	172.6467
0.025	57.4060	1.4467	4.2539	5.6870	3.7108	9.9012	172.4777
0.05	59.7791	1.4595	4.5477	6.0511	3.7029	10.2687	171.7772
0.1	63.7704	1.4722	5.1225	6.67658	3.7069	10.9409	171.5682

RESULT AND DISCUSSION:

The measured values of ultrasonic velocity, density and related thermo acoustical parameters of Atorvastatin with Water at 303K, 308 K, and 313 K temperatures in different concentrations are shown in table form .The variation of acoustical parameters with concentrations and temperature is shown graphically in fig.1 to 14. It is observed that ultrasonic velocity and acoustic impedance show nonlinear increasing variation with increase in molar concentration. This indicates that the complex formation and intermolecular weak association which may be due to hydrogen bonding. Thus complex formation can occur at these molar concentrations between the component molecules. Adiabatic compressibility (**κ**) shows an inverse behavior compared to the ultrasonic velocity. Adiabatic compressibility decreases with increase in concentration of Atorvastatin. The decrease in compressibility implies that there is an enhanced molecular association in the system with increase in solute concentration.

The opposite trend of ultrasonic velocity and adiabatic compressibility indicate that the association among interacting Atorvastatin and ethanol molecules. In the present system of Atorvastatin, free length varies nonlinearly with increase in molar concentration which suggests the significant interaction between solute and solvent due to which structural arrangement is also affected.

Relaxation time decreases with increase in concentration. Nonlinear trend of density with concentration indicates the structure-making and breaking property of solvent due to the formation and weakening of H-bonds. The free volume increases and internal pressure decreases with increases in molar concentration indicate the association through hydrogen bonding. It shows the increasing magnitude of interaction between the Atorvastatin and Ethanol.

CONCLUSION

In the present paper the ultrasonic velocity , density, viscosity and acoustical parameters, viz. adiabatic compressibility ,intermolecular free length, relaxation time, acoustic impedance , attenuation, Rao’s constant, molar volume, cohesive energy, Wada’s constant have been measured at different concentrations. The parameters indicate that there is a strong molecular interaction between unlike molecules as the concentration of drug solution increases. The molecular interaction decreases with an increase in temperature.

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