



Ultrasonic Velocity, Density and Viscosity Measurements of Some Drug in Aqueous 70% DMF at 300.15K.

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Abstract: The ultrasonic velocity (U), density (ρ) and viscosity (η) measurements have been carried out for nicotinamide, metformin hydrochloride, isoniazid, frusemide, ambroxol hydrochloride, atenolol, trimethoprim, albendazole and methyldopa in aqueous 70% Dimethylformide as a function of composition at 300.15K. Experimental data have been used to estimate the adiabatic compressibility (β), intermolecular free length (L_f), relative association (R_A) and acoustic impedance (Z). The results are discussed in terms of structure-making (or) structure-breaking effects of drug molecules in the mixtures.

Keywords: Density, Viscosity, Ultrasonic Velocity, Adiabatic Compressibility, Intermolecular Free Length, Relative Association and Acoustic Impedance.

I. Introduction

Ultrasonic is a versatile non-destructive technique and highly useful for the investigation of various physical properties. Recent developments have found use of ultrasonic energy in medicine, engineering and agriculture. Drug-macromolecular interactions are an important phenomenon in physiological media, such as blood, membranes, intra- and extracellular fluids. Physicochemical investigations play an important role in understanding the nature and the extent of the patterns of molecular aggregation that exist in binary liquid mixtures and their sensitivities to variations in composition and the molecular structure of the pure components. The drug-solvent molecular interaction play an important role in the understanding of drug action. Viscometric properties provide valuable clues for solute-solvent interactions in the solution phase. Such results can be helpful in predicting the absorption of drugs and transport of drugs across the biological membranes. Therefore, it may be interesting to investigate variation of their properties with concentration for understanding the mechanism of drug action.[1], [2], [3]

The detailed literature survey reveals that acoustical properties of the above mentioned drugs are scarce. This prompted us to investigate the acoustical properties of nine pharmacologically significant drugs, namely, Nicotinamide (NC), Metformin Hydrochloride (MH), Isoniazid (IS), Frusemide (FR), Ambroxol Hydrochloride (AH), Atenolol (AT), Trimethoprim (TM), Albendazole (AL) and Methyldopa (MT).

NC is the amide of nicotinic acid. It is a water-soluble vitamin and is part of the vitamin B group. It has anti-inflammatory property that is useful for patients with inflammatory skin conditions. It has also anxiolytic properties.[4] MH is antidiabetic drug. It is the first-line drug of choice for the treatment of type 2 diabetes, It is also used in the treatment of polycystic ovary syndrome. It is the only antidiabetic drug that has been conclusively shown to prevent the cardiovascular complications of diabetes.[5] IS is the first-line anti tuberculosis medication in prevention and treatment. It was first discovered in 1912, and it was found to be effective against tuberculosis by inhibiting its mycolic acid. It is bactericidal to rapidly-dividing mycobacteria but is bacteriostatic if the mycobacterium is slow-growing.[6] FR a sulfonamide-type drug, is used to cure hypertension and edema associated with congestive heart failure, cirrhosis, and renal disease. It is also used for hepatic cirrhosis, renal impairment and nephrotic syndrome.[7] AH is a secretolytic agent used in the treatment of respiratory diseases. It stimulates synthesis and release of surfactant by type II pneumocytes. Surfactant acts as an anti-glue factor by reducing the adhesion of mucus to the bronchial wall, in improving its transport and in providing protection against infection and irritating agents.[8] AT is a selective β_1 receptor antagonist, a drug which used primarily in cardiovascular diseases. It does not pass through the blood-brain barrier thus avoiding various central nervous system side effects.[9] TM is a bacteriostatic antibiotic mainly used in the prophylaxis and treatment of urinary tract infections.[10] AL is a benzimidazole drug used for the treatment of a variety of parasitic worm infestations. It is a broad spectrum anthelmintic, effective against roundworms, tapeworms, and flukes of domestic animals and humans. It is being used to treat lymphatic

filariasis.[11] MT is an alpha-adrenergic agonist psychoactive drug used as a sympatholytic or antihypertensive.[12]

The present work represents the continuation of a systematic investigation of the acoustical properties of drugs viz., NC, MH, IS, FR, AH, AT, TM, AL and MT in aqueous 70% DMF solutions at 300.15K. The various derived parameters such as adiabatic compressibility (β), intermolecular free length (L_f), relative association (R_A) and acoustic impedance (Z) have been calculated. The results of all these are presented and discussed below.

II. Experimental

The compounds NC (CAS No. 98-92-0), MH (CAS No. 657-24-9), IS (CAS No. 54-85-3), FR (CAS No. 54-31-9), AH (CAS No. 18683-91-5), AT (CAS No. 29122-68-7), TM (CAS No. 738-70-5), AL (CAS No. 54965-21-8) and MT (CAS No. 555-30-6) used in this study have been procured from Relief Lab Pharmaceutical. All the compounds were of 0.999 mass fraction purity. The above compounds were dried in a vacuum oven and then stored in desiccator under vacuum over fused calcium chloride before use. They were used without any further purification. Dimethylformamide used was of Analytical grade. All the mixtures were prepared in freshly prepared 70% DMF on a molarity basis by using one pan balance Dhona 200D with an accuracy ± 0.001 gm.

The density of the solutions was measured using Plunger Methods, based on Archimedes Principle using bottom loading balance (kRoy, max 100gm). The accuracy in density measurement was found to be ± 0.00001 gm. The viscometric measurement were made by Ostwald's Viscometer with an accuracy 0.001 Nsm^{-2} . The time was monitored using a stopwatch with least count of 0.1 s. All the flow time measurements are averaged over three separate measurements of the same solutions. The ultrasonic velocity was measured by using variable path single crystal interferometer (Model F-81S, Mittal Enterprises, India) at fixed frequency of 2MHz with accuracy of 0.03%. The temperature was maintained with an accuracy of 0.1°C . Electronically digital operated constant temperature bath (Plasto Craft Industries) 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 at the desired temperature with accuracy in temperature measurement -10°C to 90°C .

III. Results and Discussion

From the experimental data of density, viscosity and ultrasonic velocity of solutions (given in **Table I**), various acoustical parameters were calculated using following standard equations and given in **Table II**,

Adiabatic compressibility(β_s):

$$\beta = 1/U^2 \rho$$

Intermolecular free length (L_f):

$$L_f = K \beta^{1/2}$$

Where K is a Jacobson Constant.

Relative Association (R_A):

$$R_A = \left(\frac{\rho}{\rho_0}\right) \left(\frac{U_0}{U}\right)^{1/3}$$

Acoustic Impedance (Z):

$$Z = U \rho$$

The variation of density, viscosity, ultrasonic velocity, adiabatic compressibility, acoustic impedance, relative association and intermolecular free length of solutions as a function of molarity of solution for aq. 70% DMF at 300.15K are given in figures..

Figure 1 depicts the variation of density (ρ) of solution as a function of molarity (c) of solution for all the drug studied in the present work at $T = 300.15 \text{ K}$. It is seen from this figure that the density of solution increases continuously with the increase in molarity of solution for all the systems of drugs within the concentration range studied. Similar increase in density has also been reported by Sh. Baluja et.al in some drugs in methanol and DMF at 308.15K.[13] Figure 2 represents the variation of viscosity (η) of solution as a function of molarity (c) of solution at $T = 300.15 \text{ K}$. 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.[14] From Figure 3, it is seen that the ultrasonic velocity (U) of solution 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 suggest 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.[15]

Shown in figure 4 are the plots of adiabatic compressibility (β) of the solution versus molarity (c) of the solution at $T = 300.15$ K. It is seen from this figure 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 compressibility has also been reported by M. Selvakumar et.al in solutions of Polymethyl methacrylate & polyethyleneglycol in tetrahydrofuran.[16] Figure 5 depicts the variation of acoustic impedance (Z) of solution as a function of molarity (c) of solution for all the drug studied in the present work at $T = 300.15$ K. The acoustic impedance increases with increase in solute concentration. Theoretical requirement of Z is density and velocity which are increased with increase of concentration of solute in solution. The increase of Z with solute concentration can be attributed to the effective solvent-solute interactions. Similar increase in acoustic impedance has also been reported by B. R. Shinde et.al in aqueous manganous chloride solution at different temperatures.[17]

Figure 6 represents the plots of intermolecular free length (L_f) of the solution versus molarity (c) of the solution at $T = 300.15$ K. It is seen from this figure that the value of the ultrasonic velocity depends on intermolecular free length. The velocity increases with decrease in L_f or vice versa. L_f decreases continuously which suggest that there is strong interaction between solvent and drug molecules. Similar decrease in intermolecular free length has also been reported by J. D. Pandey et.al during the study of Intermolecular free length & free volume of pure liquids at varying temperatures & pressures.[18] Figure 7 represents the plots of relative association (R_A) of the solution versus molarity (c) of the solution at $T = 300.15$ K. It is seen that the relative association depends on either the breaking up of the solvent molecules on addition of solute to it or the salvation of ions that are present. The relative association value shows increase with the increase of solute concentration. This increase is due to the solute-solvent interaction dominates over solvent-solvent interactions. Similar increase in relative association has also been reported by A. Tadkalkar et.al during the ultrasonic studies on interaction of inorganic salts with fructose.[19]

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Table I: Density (ρ), ultrasonic velocity (U) and viscosity (η) of solutions at T = 300.15K.

Solute	c, M	ρ , kg m ⁻³	U, m s ⁻¹	η , N s m ⁻²
NC	0.001	985.4875	1646.267	1.23018
	0.002	985.5779	1646.867	1.248934
	0.003	985.7078	1647.233	1.25842
	0.004	985.9019	1647.867	1.267991
	0.005	986.0489	1648.267	1.277505
MH	0.001	985.998	1646.267	1.240142
	0.002	986.1224	1647.267	1.249624
	0.003	986.5298	1648.533	1.259469
	0.004	986.6676	1649.267	1.278307
	0.005	986.9885	1650.333	1.288056
IS	0.001	985.6814	1646.267	1.239744
	0.002	985.7775	1647.067	1.249187
	0.003	985.9207	1647.867	1.258692
	0.004	986.1186	1648.267	1.277596
	0.005	986.3544	1648.867	1.287229
FR	0.001	986.8526	1649.067	1.371871
	0.002	987.0584	1650.267	1.40016
	0.003	987.3229	1651.267	1.428546
	0.004	987.4571	1652.067	1.447417
	0.005	987.6784	1653.733	1.466422
AH	0.001	987.0584	1650.267	1.418829
	0.002	987.2606	1651.733	1.456465
	0.003	987.563	1652.867	1.484929
	0.004	987.79	1653.533	1.522635
	0.005	987.9735	1654.867	1.550947
AT	0.001	986.3751	1647.733	1.324568
	0.002	986.6827	1648.533	1.343642
	0.003	986.8337	1649.867	1.381177
	0.004	986.9092	1650.867	1.409282
	0.005	987.2039	1651.267	1.43771
TM	0.001	986.5525	1648.267	1.343465
	0.002	986.8337	1649.067	1.371845
	0.003	986.9678	1650.267	1.390698
	0.004	987.0528	1651.533	1.428155
	0.005	987.2228	1652.067	1.447073
AL	0.001	986.311	1647.533	1.315154
	0.002	986.6279	1648.267	1.343568
	0.003	986.7393	1649.267	1.371714
	0.004	986.8771	1650.267	1.39057
	0.005	987.117	1651.067	1.418913

MT	0.001	986.1224	1647.067	1.286926
	0.002	986.3487	1647.733	1.315204
	0.003	986.4732	1648.867	1.343357
	0.004	986.7091	1649.867	1.36234
	0.005	987.0433	1650.267	1.38147

Table II: Variation of thermodynamic parameters at different concentrations & T = 300.15K.

Solute	c, M	$\beta \times 10^{-10}, \text{m}^2\text{N}^{-1}$	$Z \times 10^6, \text{Nm}^{-2}$	$L_b, \text{\AA}$	R_A
NC	0.001	3.744108	1.6223	0.3991	0.999568
	0.002	3.741036	1.6231	0.3990	0.999538
	0.003	3.738882	1.6236	0.3989	0.999596
	0.004	3.73527	1.6246	0.3987	0.999665
	0.005	3.732901	1.6252	0.3985	0.999733
MH	0.001	3.742169	1.6232	0.3990	1.000079
	0.002	3.737156	1.6244	0.3988	0.999902
	0.003	3.729877	1.6263	0.3984	0.999931
	0.004	3.726037	1.6272	0.3982	0.999848
	0.005	3.720015	1.6288	0.3978	0.99985
IS	0.001	3.743371	1.6226	0.3991	0.999765
	0.002	3.739371	1.6236	0.3989	0.9997
	0.003	3.735199	1.6246	0.3987	0.999684
	0.004	3.732637	1.6253	0.3985	0.999803
	0.005	3.729029	1.6263	0.3983	0.999921
FR	0.001	3.726243	1.6273	0.3982	1.000096
	0.002	3.720049	1.6289	0.3978	0.999941
	0.003	3.71455	1.6303	0.3976	0.999906
	0.004	3.710449	1.6313	0.3973	0.999799
	0.005	3.702147	1.6333	0.3969	0.99952
AH	0.001	3.720049	1.6289	0.3978	0.999941
	0.002	3.712688	1.6306	0.3975	0.999701
	0.003	3.70646	1.6323	0.3971	0.999665
	0.004	3.702624	1.6333	0.3969	0.999693
	0.005	3.695971	1.6349	0.3966	0.999476
AT	0.001	3.734085	1.6252	0.3986	1.000016
	0.002	3.729299	1.6265	0.3983	1.000085
	0.003	3.722701	1.6281	0.3980	0.999834
	0.004	3.717908	1.6292	0.3977	0.999608
	0.005	3.714998	1.6301	0.3976	0.999785
TM	0.001	3.730995	1.6261	0.3984	1.000034
	0.002	3.726314	1.6273	0.3982	1.000077
	0.003	3.720391	1.6287	0.3979	0.999849
	0.004	3.71437	1.6301	0.3975	0.999551
	0.005	3.71133	1.6309	0.3974	0.999562
AL	0.001	3.735235	1.6249	0.3987	1.000012
	0.002	3.73071	1.6262	0.3984	1.000111
	0.003	3.725767	1.6273	0.3982	0.99992
	0.004	3.720733	1.6286	0.3979	0.999757
	0.005	3.716225	1.6297	0.3976	0.999758
MT	0.001	3.738063	1.6242	0.3988	0.999962
	0.002	3.734185	1.6252	0.3986	0.99999
	0.003	3.72858	1.6265	0.3983	0.999772
	0.004	3.723171	1.6279	0.3980	0.999708
	0.005	3.720106	1.6288	0.3979	0.999925

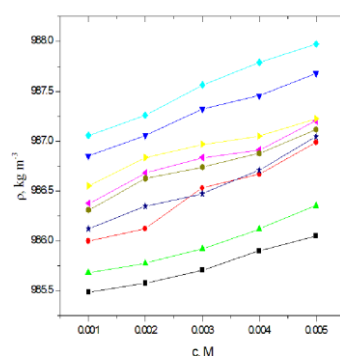
Figure 1: Variation of Density with Concentration of solutions at T = 300.15K.

Figure 2: Variation of Ultrasonic Velocity with Concentration of solutions at T = 300.15K.

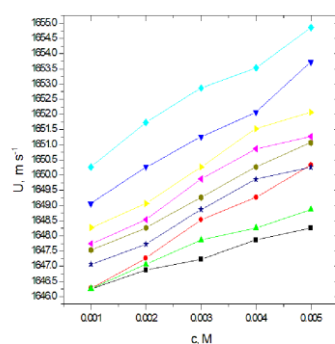


Figure 3: Variation of Viscosity with Concentration of solutions at T = 300.15K.

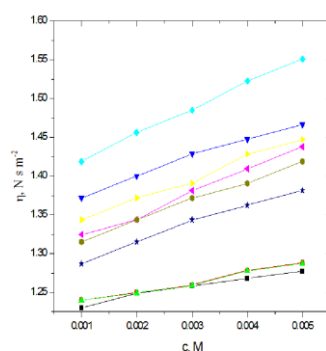


Figure 4: Variation of Adiabatic Compressibility with Concentration of solutions at T = 300.15K.

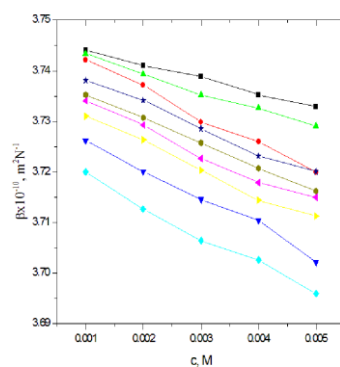


Figure 5: Variation of Acoustic Impedance with Concentration of solutions at T = 300.15K.

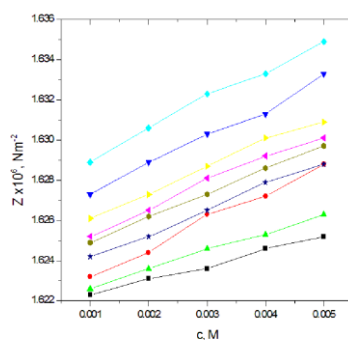


Figure 6: Variation of Intermolecular Free Length with Concentration of solutions at T = 300.15K.

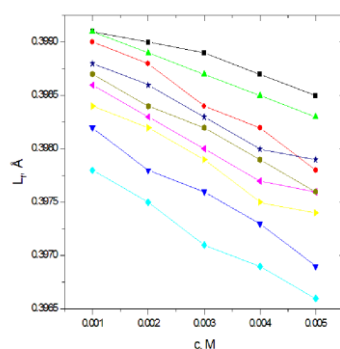
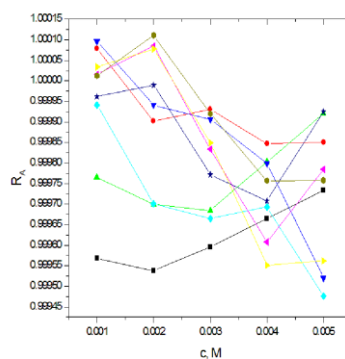


Figure 7: Variation of Relative Association with Concentration of solutions at T = 300.15K.



Plots of variation in acoustical parameters of solute in the solution against molarity of aqueous 70% dimethylformamide solutions of different drugs at T = 300.15 K: Lines: Black: NC, Bright Green: IS, Red: MH, Dark Blue: MT, Dark Yellow: AL, Pink: AT, Yellow: TM, Blue: FR and Turquoise: AH.