Journal of Global Biosciences
ISSN 2320-1355
Volume 4, Number 2, 2015, pp. 1530-1542
Website: www.mutagens.co.in
E-mail: submit@mutagens.co.in
researchsubmission@hotmail.com

Research Paper

ULTRASONIC VELOCITY AND ACOUSTICAL PARAMETERS OF HYBRID DRUGS OF AMBROXOL HYDROCHLORIDE AT 300.15 K

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Abstract

The density (ρ), viscosity (η) and ultrasonic velocity (U) (2 MHz) of 70% DMF-Water and 70% Methanol-Water solutions of synthesized hybrid drugs, have been investigated in order to understand the effect of solvents on molecular interactions in these systems at300.15 K. Various acoustical parameters such as the adiabaticcompressibility (κ_s), intermolecular freepath length (L_f), Rao's molar constant (Rm), Wada's constant (W), acoustic impedance (Z), relative association (R_A) andviscous relaxation time (τ) have been determined and correlated withthe concentration (C). Good-to-excellent correlations are observed between a given parameterand the concentration. Linear or nonlinear increases or decreases of acousticalparameters with concentration indicated the existence of strong molecular interactions inthe solutions.

Key words: Density, Viscosity, Ultrasonic velocity, Acoustical parameters,Molecular interactions, hybrid drugs.

INTRODUCTION

Nowaday, ultrasonic technology is employed in diverse fields in investigating variousorganic liquids, polymers and their mixtures, drugs, aqueous and non-aqueous electrolyte solutions etc. It plays an important role in understanding the physico-chemical behavior of liquids [1-5]. Knowledge of the ultrasonic velocity and related acoustical parameters provides informationabout molecular interactions, the nature and strength of these interactions are very useful in solution processing technology. The study on changes in acoustical properties of solutions has beenfound to be an excellent qualitative and quantitative way to bring out the information about molecular structure andintermolecular forces present in the liquid mixtures[6-10].

Ambroxol hydrochloride (*4-[[(2-Amino-3, 5-dibromo-phenyl) methyl] amino]-cyclohexanol hydrochloride*) which is a semi synthetic derivative of vasicine from the Indian shrub "*Adhatodavasica*". It is an active expectoration improver and acts as a potent mucolytic agent. It is used as a bronchosecretolytic and expectorant drug hence used in the treatment of bronchial

asthama and chronic bronchitis. It stimulates the transportation of the viscous secretion in the respiratory organs and reduces the stand stillness of the secretion. It has also been reported to have a cough suppressing effect and anti-inflammatory action. Recently the inhibition of nitric oxide dependent activation of soluble guanylate cyclase was suggested one of the molecular mechanism of the therapeutic action of ambroxol hydrochloride, also used in pulmonary alveolar proteinosis in pulmonary distress and infant respiratory distress syndrome[11,12]. Taking in view of the applicability of ambroxol hydrochloride by pharmaceutical aspect, in present chapter, work was undertaken to synthesized some new hybrid drugs of ambroxol hydrochloride and other bioactive compounds having better drug potential and studied their acoustical parameters in 70% DMF-Water and 70% Methanol-Water systems and to throw light on solute-solvent interactions.

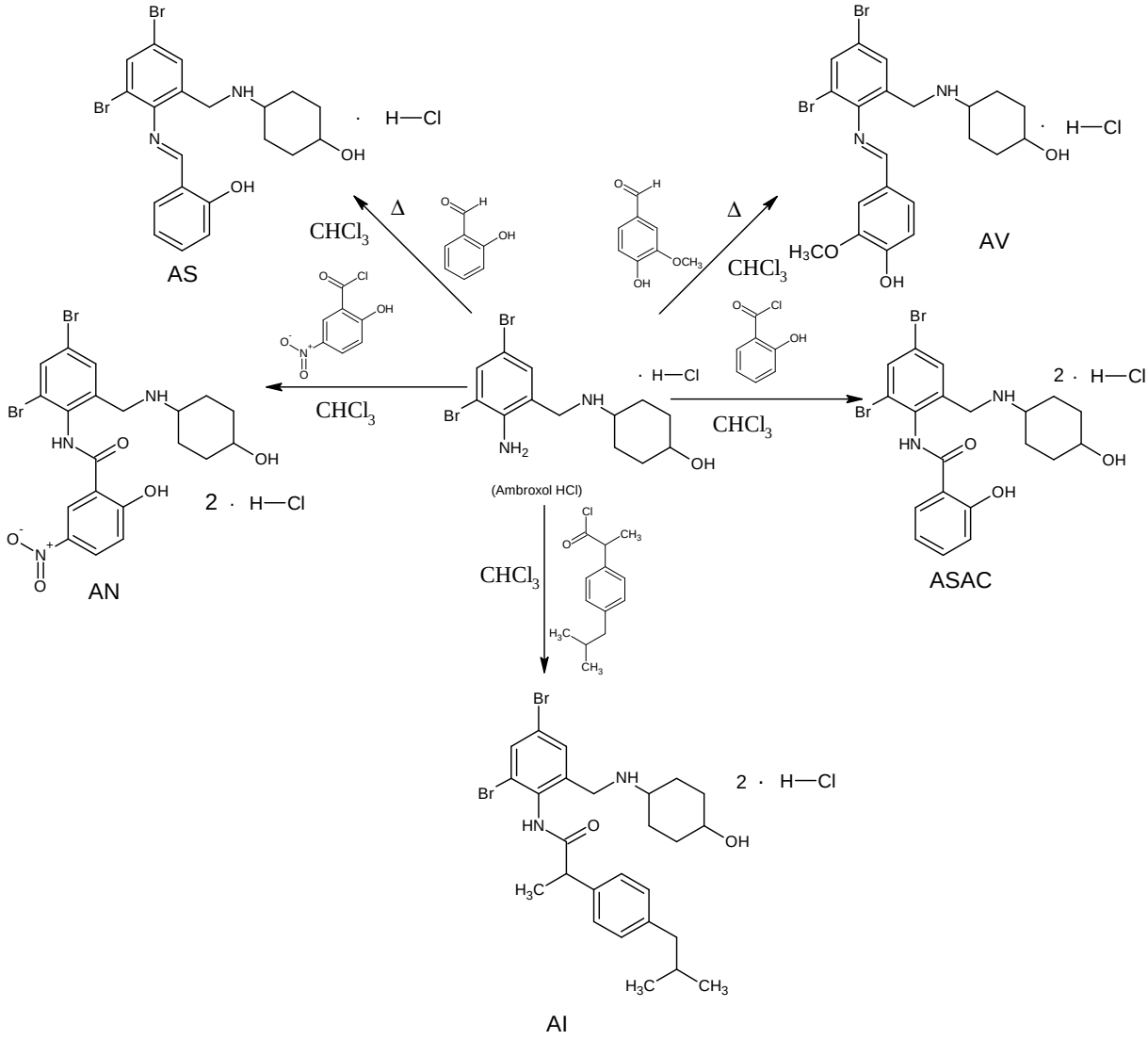
MATERIALS AND METHODS

In the present study, thesolutes were used which were synthesized by using following reactants,Ambroxol Hydrochloride and Ibuprofen procured from Relief Lab Pvt. Ltd., Kalmeshwar (minimum assay 99.5 %) were used without any pretreatment, after drying it in a vacuum oven. Salicylic Acid, Salicylaldehyde and 5-Nitro Salicylic Acid were procured from S.D.Fine Chemicals, India. Vanillin was procured from Merck.

The solvent used for synthesis of above hybrid drug (chloroform) was purified by fractional distillation and the middle fractions were collected.For physico-chemical study analytical grade solvents: N,N-Dimethyl Formamide and Methanol, were used. Theywere purified and fractionally distilled prior to their use. Double distilled water used for making systems [13].

The condensation of ambroxol hydrochloride with acid chlorides of salicylic acid, 5-nitro salicylic acid and ibuprofen by shaking in the presence of chloroform medium for about 3-4hrs. has resulted in the formation of *N-(2-((4-hydroxycyclohexylamino)methyl)-4,6-dibromophenyl)-2-hydroxybenzamide dihydrochloride*(ASAC), *N-(2-((4-hydroxycyclohexylamino)methyl)-4,6-dibromophenyl)-2-hydroxy-5-nitrobenzamidedihydrochloride*(AN) *and N-(2-((4-hydroxycyclohexylamino)methyl)-4,6-dibromophenyl)-2-(4-isobutylphenyl)propanamidedihydrochloride* (AI) respectively.

The nicotinamide refluxed with salicylaldehyde and vanillin in the presence of chloroform medium for about 2-3hrs. has resulted in the formation of *(E)-2-((2,4-dibromo-6-((4-hydroxycyclohexylamino)methyl)phenylimino)methyl)phenolhydrochloride* (AS) *and(E)-4-((2,4-dibromo-6-((4-hydroxycyclohexylamino)methyl)phenylimino)methyl)-2-methoxyphenolhydrochloride* (AV) respectively.



All the synthesized solutes were crystallized using suitable solvent and characterized by IR and ^{1}H NMR Spectra. The physical constant and spectral data of drugs are summarized in Tables 1 and 2.

The density (ρ), viscosity (η), and ultrasonic velocity (U) measurements on the solutions were carried out at 300.15 K (Low Temperature Bath Model-LTB-10)by using a Digital Densitimeter (Model DDM 2910, Rudolph Research Analytical, USA), an Ostwald Viscometer, and a MittalEnterprise Ultrasonic Interferometer (New Delhi), Model No. F-81S, operating at 2 MHz, respectively. Measured values of ρ, η and U for the solutionswere summarized in Table 3.

RESULTS AND DISCUSSION

The ρ, η and U values increased linearly with concentration (C). The densitiesof the solutions increase with C. Thus, the rule of additivity of density is observed.The ρ, η and U data were correlated with the concentration C and found to have a fairly good-to-excellent correlation between agiven parameter.The variation of η and U with C is considerably more than that of ρ due to specificmolecular interactions. Molecular interactionsdepend on the strength of the repulsive forces acting amongst solvent and solute molecules and hence intermolecular motion is affected accordingly. Attractive forces resultin molecular association (solvation), i.e. modification of the solute molecules. Molecular associationleads to changes in both the apparent molecular volume as well as mass, andhence the density changes accordingly. Thus ρ, η and U values are affected by molecular interactions under a given set of experimental

conditions. From the measured data ofρ, η and Usome acoustical parameters were derived which summarized in Tables 4 and 5.

The variation of adiabatic compressibility with concentration is shown in Figures3 and4 wherevalues are found to decrease with concentration for all the drugs in both the solvents. When solute is added to a solvent, it attracts certain solvent molecules towards itself and hence less number of solvent molecules will be made available for the next incoming species. Due to the aggregation of solvent molecules around the solute, the adiabatic compressibility decreases with increase in concentration of solute supporting solute-solvent interaction. The decrease in adiabatic compressibility is attributed to the fact that the drug molecules in solutions are considerably ionized and these ions are surrounded by a layer of solvent molecules firmly bound and oriented toward the ions. Decrease in adiabatic compressibility indicates the formation of large number of tightly bound systems. In 70% DMF-Water system, magnitude of adiabatic compressibility values are lower suggesting that solute-solvent interactions are strong as compared to 70% Methanol-Water system [14]. Intermolecular free length depends on the intermolecular attractive and repulsive forces. It is evident from Figures 5 and 6 that $L_f$decreases continuously. Continuous decrease of adiabatic compressibility and intermolecular free length is a clear evidence of strong interactions between solvent and compound molecules. Such interactions may be due to dipole-dipole, dipole-induced-dipole interactions. The intermolecular free length in 70% DMF-Water shows the lower values suggesting that the solute and solvent molecules are moving towards each other resulting in stronger solute-solvent interaction as compared to 70% Methanol-Water system [15].

Tables 4 and 5 shows Rao's constant, also known as molar sound function, increases with increasing concentration indicates that there is strong interaction between solute and solvent molecules. Wada's constant also known as molar adiabatic compressibility may be considered for existing interaction. The values of Wada's constant increase with increasing concentration indicate that there must be tight packing of the medium and hence interaction is increasing. Thus there may be solute-solvent interaction occurring [16,17]. The product of ultrasonic velocity and density is known as "specific acoustic impedance" of the medium. This factor is governed by the inertial and elastic properties of the medium. From Tables 4 and 5, it is evident that acoustic impedance increases with increase in concentration of solute for all the solutes in both the solvents. This is in agreement with the theoretical requirements as velocity and density both increase with increasing concentration of solute in solution. The increase of Z values with solute concentration can be attributed to the powerful solute-solvent interactions. The values of acoustic impedance in 70% DMF-Water are higher than in 70% Methanol-Water supporting the findings that the solute-solvent interaction is stronger in 70% DMF-Water system[18].

Table 4 and 5 shows the variation of relative association (R_A) with concentration in 70% DMF-Water and 70% Methanol-Water. The values of density and ultrasonic velocity enable to calculate the relative association. Relative association is influenced by two important factors: 1) Breaking up of the associated solvent molecules on addition of solute into it. This leads to the decrease of relative association.2) The solvation of solute molecules that is simultaneously present. This leads to the increase of relative association.Relative association decreases with increase in concentration for all the solutes. This may be due to the breaking up of the associated solvent molecules on addition of solute which indicates the structure-forming tendencies of solutes decreases at higher concentration in both the solvents. The values are lower in 70% Methanol-Water system as compared to 70% DMF-Water system. This suggests that the structure-making tendency of the solutes is enhanced in 70% DMF-Water [19]. Viscous relaxation time (τ) increases on increasing the concentration of solute as shown in Tables 4 and 5 which indicates the presence of molecular interactions. Increasing trend of τ with concentration supports structure making capacity of the solute. This parameter is the cumulative effect of ultrasonic velocity, density and viscosity of solution under the given sets of conditions. Thus, it is suggested that the molecules get re-arranged due to co-operative process. The compounds ASAC, AS, AV, AN and AI in 70% Methanol-Water system shows increase in relaxation time value at lower concentration and then it dropped suddenly and then it increases

further with concentration in case of AI and AS and becomes almost constant in case of AN, ASAC and AV [20].

Thus, the nature of the solvents and solute play importantroles in determining transport and other physico-chemical properties.The ultrasonic velocity in the solutions depends on the intermolecular free path length.When ultrasonic waves are incident on the solution, the molecules become perturbed. Dueto some elasticity of the medium, perturbed molecules regain their equilibrium positions.When a solute is added to a solvent, its molecules attract certain solvent molecules towardsthem. The phenomenon is known as compression. The aggregation of solvent moleculesaround solute molecules supports the presence of powerful solvent–solute interactions. Becauseof solvent–solute interactions, the structure of the solute is modified to a considerableextent. Relaxation processes cause dispersion of the ultrasonic speed in the system. Molecular interactions such as solvent–solute interactions, quantum mechanical dispersive forces,and the dielectric force may cause either contraction or expansion and, as a consequence,the transport properties of the solutions will be altered with concentration.

CONCLUSION

The synthesized hybrid drugs might show cumulative effect. They may be pertaining the pharmacological activity of parent drug with substantial analgesic and antipyretic activity of salicylic acid, 5-nitro salicylic acid, salicylaldehyde, ibuprofen and antioxidant activity of vanillin. Hybrid drugs of ambroxol hydrochloride might show their own pharmacological activity as expectorant. Fairly good correlations are observed between the studied parameters and concentration.The linear or nonlinear increases or decreases of acoustical parameters indicate theexistence of strong molecular interactions in the solutions that depend on the molecularstructure. In both 70% DMF-Water and 70% Methanol-Water system, solute-solvent interaction predominates over solute-solute interaction. But 70% DMF-Water system shows large extent of solute-solvent interaction due to structural difference of both the solvent.

Table 1: Physical constants of drugs.

Sr.No.	Comp.	R	M.F.	M. Wt. (g/mol)	R_f* Value	M.P. ^{0}C	Yield %
1	ASAC	Ethanol	$C_{20}H_{24}Br_2Cl_2N_2O_3$	571.13	0.784	198-199	77
2	AS	Ethanol	$C_{20}H_{23}Br_2ClN_2O_2$	518.66	0.684	222-223	72
3	AV	Ethanol	$C_{21}H_{25}Br_2ClN_2O_3$	548.69	0.750	227-228	69
4	AN	Ethanol	$C_{20}H_{23}Br_2Cl_2N_3O_5$	616.12	0.650	230-231	70
5	AI	Ethanol	$C_{26}H_{36}Br_2Cl_2N_2O_2$	639.29	0.725	234-235	72

*Ethyl Acetate:Ethanol 3:7

Table 2: IR spectral data of drugs.

Vibration Mode		*ν, (cm^{-1})*				
		ASAC	**AS**	**AV**	**AN**	**AI**
br. OH		3400	3396	3410	3452	3429
-NH		3350	3286	3310	3352	3331
Aromatic ring str.	**C-H str.**	3180	3150	3120	3050	3016
	C=C	1668	1633	1630	1668	1633
	C-H i.p.def.	1130	1120	1110	1130	1168
	C-H o.o.p.def	821	823	821	829	821
C=O		1700	1790	1680	1700	1714
C-N		1224	1284	1269	1284	1269
C=N		1580	1600	1590	1630	1600

Table 3: Ultrasonic Velocities, Densities and Viscosities of hybrid drugs of ambroxol hydrochloride in 70% DMF-Water and 70% Methanol-Water solutions at T=300.15 K.

	70% DMF-Water			70% Methanol-Water		
Conc. M	**Density ρ g.cm^{-3}**	**Velocity U. 10^{-5}cm.s^{-1}**	**Viscosity η. 10^{3} poise**	**Density ρ g.cm^{-3}**	**Velocity U. 10^{-5}cm.s^{-1}**	**Viscosity η. 10^{3} poise**
ASAC						
0.001	0.98696	1.6512	15.02689	0.881504	1.4234	31.36749
0.002	0.987351	1.6537	15.40633	0.881568	1.4337	31.6507
0.003	0.987692	1.6572	15.59845	0.882182	1.4417	31.86013
0.004	0.987746	1.6617	15.87955	0.882312	1.4477	32.146
0.005	0.987883	1.6657	16.162	0.882359	1.4546	32.52263
AS						
0.001	0.987329	1.6524	16.15294	0.880887	1.4195	30.69055
0.002	0.987605	1.6568	16.34424	0.881355	1.4297	30.8941
0.003	0.987998	1.6598	16.63105	0.881865	1.4386	31.19298
0.004	0.988142	1.6641	17.00726	0.88199	1.4439	31.38478
0.005	0.988339	1.6687	17.29105	0.882115	1.4491	31.76404
AV						
0.001	0.986688	1.6492	13.99635	0.881267	1.4219	31.07824
0.002	0.987181	1.6517	14.28341	0.881496	1.4309	31.36719
0.003	0.987276	1.6546	14.47151	0.881992	1.4403	31.57222
0.004	0.987533	1.6597	14.84883	0.882088	1.4454	31.85676
0.005	0.987773	1.6631	15.22609	0.8822	1.4516	32.04822
AN						
0.001	0.98745	1.6542	16.52844	0.881878	1.4256	32.22387
0.002	0.987815	1.6591	16.72138	0.88191	1.4359	32.50608
0.003	0.988221	1.6621	17.00863	0.882475	1.4434	32.71436
0.004	0.988373	1.6669	17.38511	0.882521	1.4496	32.99728
0.005	0.98853	1.6709	17.57484	0.882597	1.4569	33.18764
AI						
0.001	0.988076	1.6561	18.31428	0.881997	1.4275	32.88401
0.002	0.988441	1.6611	18.50801	0.882127	1.4372	33.07628
0.003	0.988833	1.6652	18.8894	0.882597	1.4454	33.37514
0.004	0.988972	1.6687	19.07909	0.882663	1.4507	33.75267
0.005	0.989154	1.6734	19.36323	0.882789	1.4591	34.13255

Table 4: Acoustical properties of hybrid drugs in 70% DMF-Water solutions at T=300.15 K.

Conc. M	κ_s x10^{-10} cm^2dyn^{-1}	L_f Å	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$Z.10^{-5}$ $g.cm^{-2}$	$\tau.10^{-6}$ s	R_A	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$
ASAC							
0.001	3.634729	1.243756	6.839053	1.650511	11.29959	1.000154	6.665241
0.002	3.610577	1.239617	6.846028	1.656087	11.36064	0.999135	6.671067
0.003	3.596252	1.237155	6.845533	1.659905	11.45748	0.999208	6.670653
0.004	3.579923	1.234344	6.849622	1.663801	11.54124	0.998611	6.674068
0.005	3.556003	1.230213	6.856926	1.669425	11.64238	0.997547	6.680168
AS							
0.001	3.649702	1.246315	6.211914	1.646506	10.97338	0.999966	6.053877
0.002	3.623901	1.241902	6.215672	1.652765	10.99167	0.999362	6.057017
0.003	3.609635	1.239455	6.215457	1.65652	11.09014	0.999396	6.056837
0.004	3.594132	1.236791	6.219025	1.66019	11.17855	0.998823	6.059817
0.005	3.565934	1.23193	6.226218	1.666854	11.22598	0.997669	6.065824
AV							
0.001	3.641523	1.244918	6.570652	1.648717	11.18088	1.000107	6.403618
0.002	3.618492	1.240975	6.575837	1.654146	11.20307	0.999319	6.407949
0.003	3.6034	1.238384	6.575881	1.658097	11.34299	0.999312	6.407985
0.004	3.588459	1.235814	6.579699	1.661625	11.43154	0.998732	6.411174
0.005	3.559971	1.230899	6.587559	1.668356	11.47553	0.99754	6.417739
AN							
0.001	3.629434	1.24285	7.376327	1.652027	11.74071	1.000353	7.189064
0.002	3.60294	1.238305	7.385125	1.65811	11.79029	0.999161	7.196413
0.003	3.587785	1.235698	7.384851	1.662136	11.92751	0.999198	7.196184
0.004	3.575703	1.233616	7.388689	1.664972	12.02185	0.998679	7.19939
0.005	3.548439	1.228904	7.397706	1.671396	12.06381	0.997462	7.20692
AI							
0.001	3.623289	1.241797	7.654668	1.65354	12.03925	1.000229	7.460207
0.002	3.596445	1.237189	7.662907	1.659816	12.04159	0.999154	7.467089
0.003	3.583834	1.235018	7.662653	1.663175	12.14012	0.999187	7.466876
0.004	3.568995	1.232458	7.667059	1.666712	12.22492	0.998613	7.470557
0.005	3.539806	1.227408	7.67632	1.673685	12.25939	0.997408	7.478291

Table 5: Acoustical properties of hybrid drugs in 70% Methanol-Water solutions at T=300.15 K.

Conc. M	κ_s x10^{-10} cm^2dyn^{-1}	L_f Å	$Rm.10^{-3}$ $cm^{-8/3}.s^{-1/3}$	$Z.10^{-5}$ $g.cm^{-2}$	$\tau.10^{-6}$ s	R_A	$W.10^{-3}$ $cm^{-1}.dyn^{-1}$
ASAC							
0.001	5.599145	1.54369	7.288189	1.254733	23.41749	0.994791	7.038713
0.002	5.518581	1.532544	7.305193	1.263905	23.28893	0.992476	7.052787
0.003	5.453713	1.52351	7.313669	1.271841	23.16746	0.991326	7.0598
0.004	5.4078	1.517084	7.322718	1.277323	23.17855	0.990101	7.067286
0.005	5.356329	1.509847	7.333939	1.28348	23.22692	0.988586	7.076568
AS							
0.001	5.633899	1.548473	6.617202	1.250419	23.05433	0.995005	6.390889
0.002	5.550846	1.537018	6.629489	1.260074	22.86512	0.99316	6.40106
0.003	5.47921	1.527067	6.639379	1.268651	22.78838	0.991681	6.409244
0.004	5.438286	1.521354	6.646578	1.273505	22.75726	0.990607	6.4152
0.005	5.398559	1.515787	6.653602	1.278273	22.86401	0.989561	6.42101
AV							
0.001	5.612473	1.545526	7.001253	1.253074	23.25677	0.994874	6.761678
0.002	5.540657	1.535606	7.014175	1.261332	23.17265	0.993041	6.772375
0.003	5.465496	1.525155	7.025548	1.270333	23.00771	0.991433	6.781785
0.004	5.4264	1.51969	7.03306	1.27497	23.04901	0.990374	6.788
0.005	5.379463	1.513104	7.042209	1.280602	22.98696	0.989088	6.795568
AN							
0.001	5.579509	1.540981	7.863017	1.257206	23.97245	0.994701	7.593767
0.002	5.49955	1.529899	7.881621	1.266335	23.83584	0.992354	7.609164
0.003	5.439065	1.521463	7.890271	1.273764	23.72474	0.991266	7.616321
0.004	5.392359	1.514916	7.901142	1.279302	23.72442	0.989902	7.625315
0.005	5.337994	1.50726	7.913698	1.285855	23.62072	0.988331	7.6357
AI							
0.001	5.563918	1.538826	8.161242	1.25905	24.39519	0.994394	7.881431
0.002	5.488256	1.528327	8.178476	1.267793	24.20414	0.992298	7.895694
0.003	5.423273	1.519253	8.189641	1.275706	24.13366	0.990945	7.904932
0.004	5.383315	1.513645	8.199024	1.280479	24.22683	0.989811	7.912695
0.005	5.320754	1.504824	8.21365	1.288077	24.21479	0.988049	7.924792

Figure 1: IR Spectra of *N-(2-((4-hydroxycyclohexylamino)methyl)-4,6-dibromophenyl)-2-hydroxybenzamide dihydrochloride.*

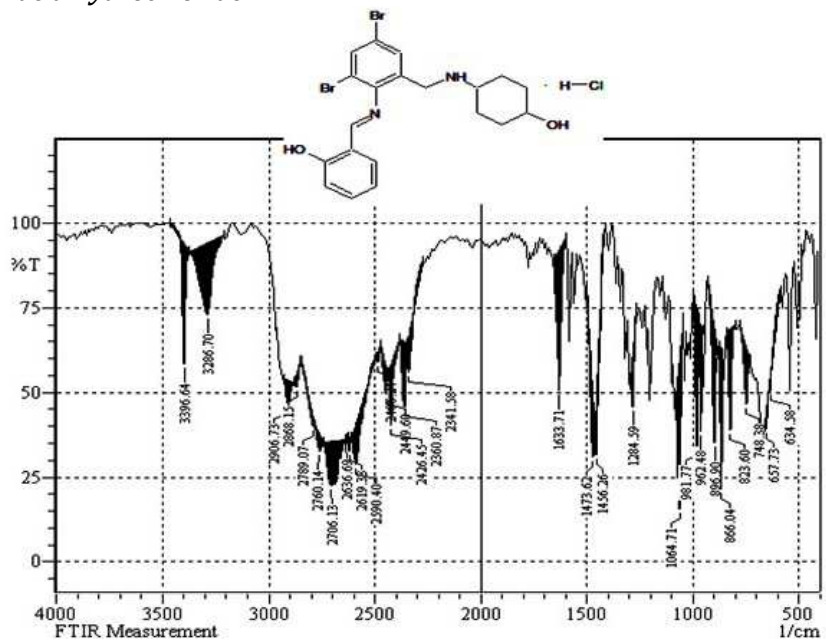
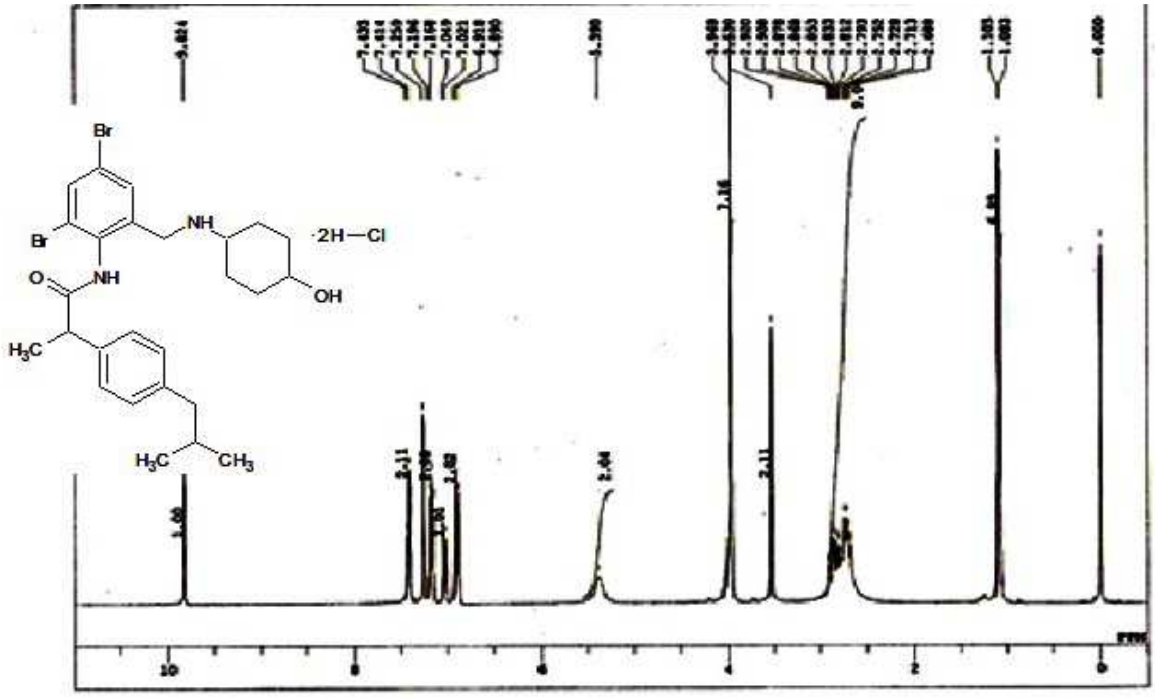


Figure 2: ^{1}HNMR Spectra of *N-(2-((4-hydroxycyclohexylamino)methyl)-4,6-dibromophenyl)-2-(4-isobutylphenyl)propanamidedihydrochloride*.



AI: ^{1}HNMR ($CDCL_3$) δ: 9.824(1H, OH), 7.433-7.414(2H, NH), 7.259-6.890(6H, Aromatic), 3.969-3.530(2H, Ar-CH_2-NH), 2.920-2.908(2H, Ar-CH_2), 2.878-2.688(15H, Cyclohexyl, -CH, Ar-CH-CH_3), 1.103-1.083(6H, Aliphatic).

Figure 3: Variation of Adiabatic Compressibility with Concentration in 70% DMF-Water at 300.15 K.

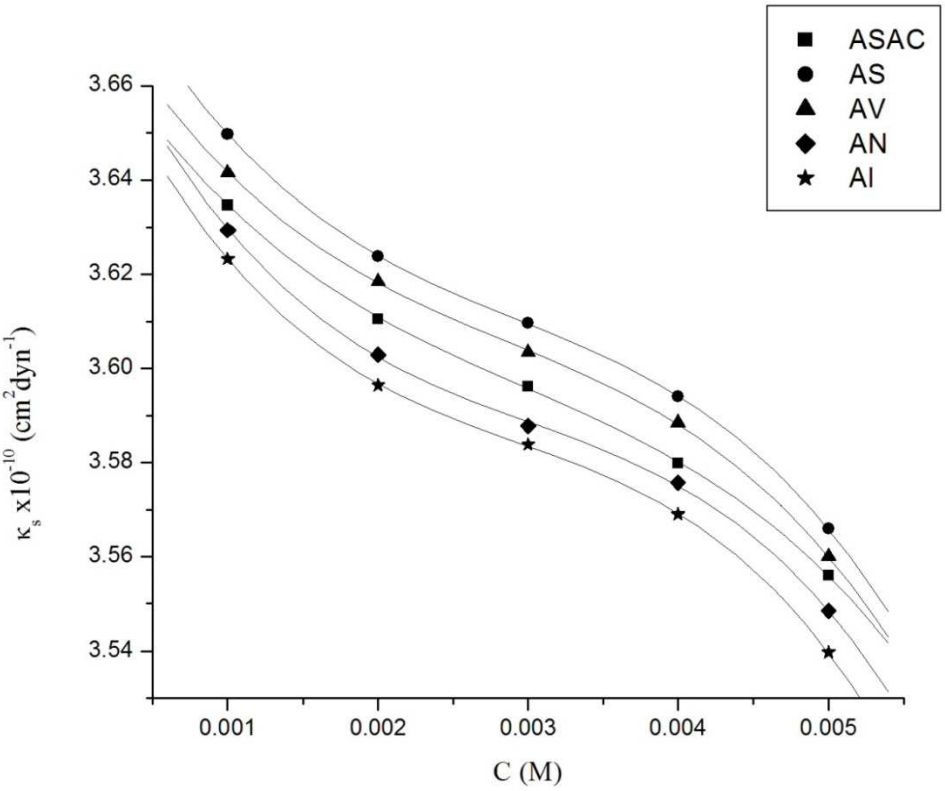


Figure 4: Variation of Adiabatic Compressibility with Concentration in 70% Methanol-Water at 300.15 K.

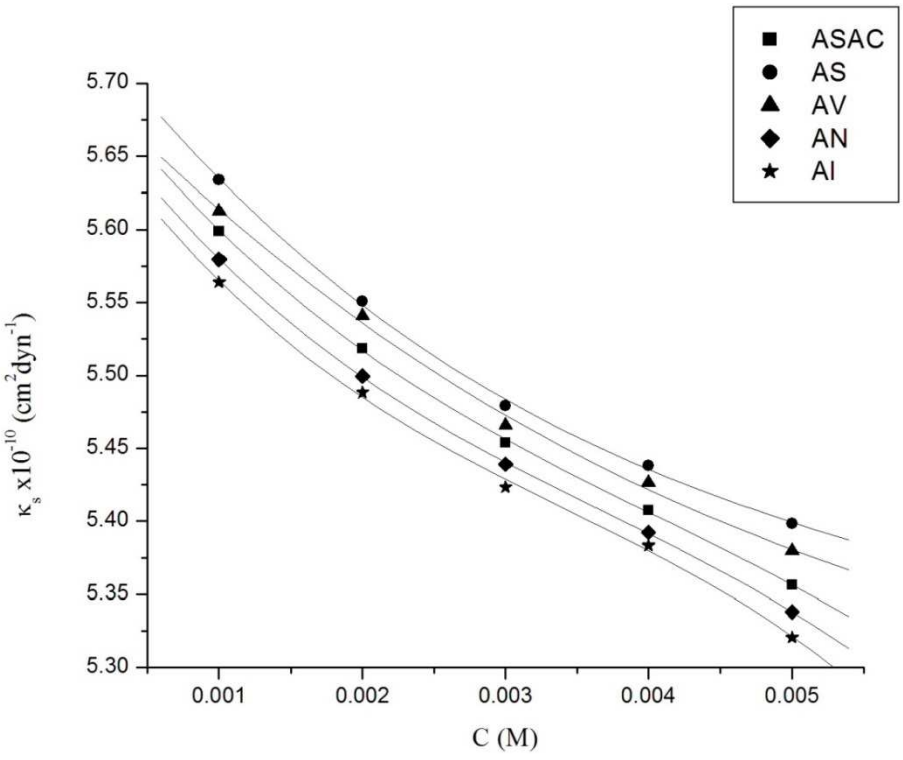


Figure 5: Variation of Intermolecular Free Length with Concentration in 70% DMF-Water at 300.15 K.

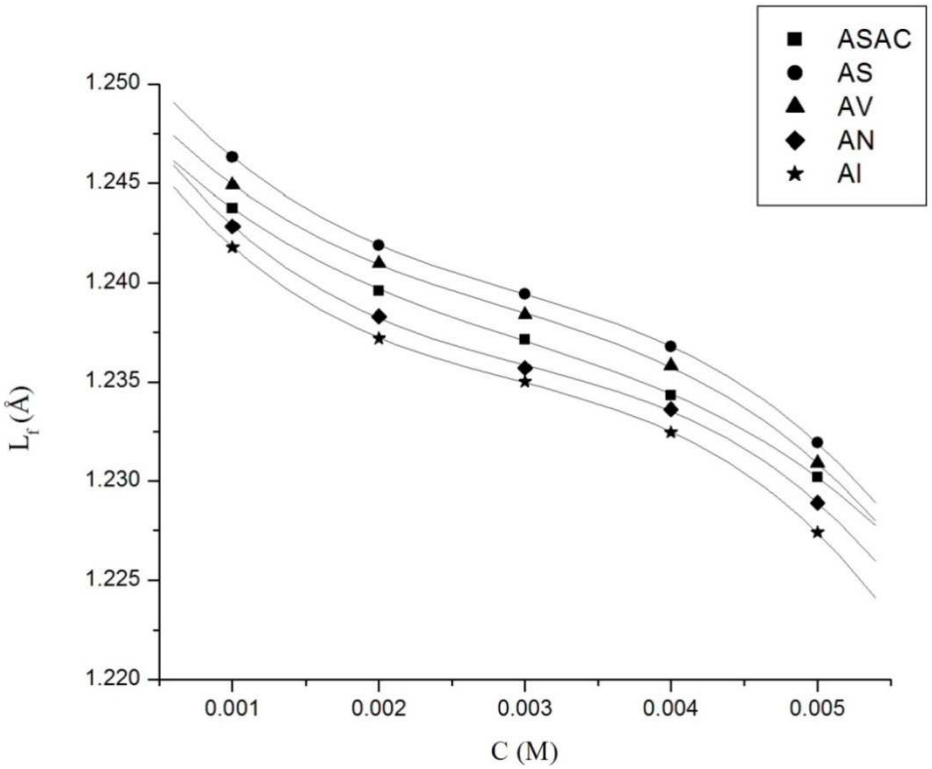
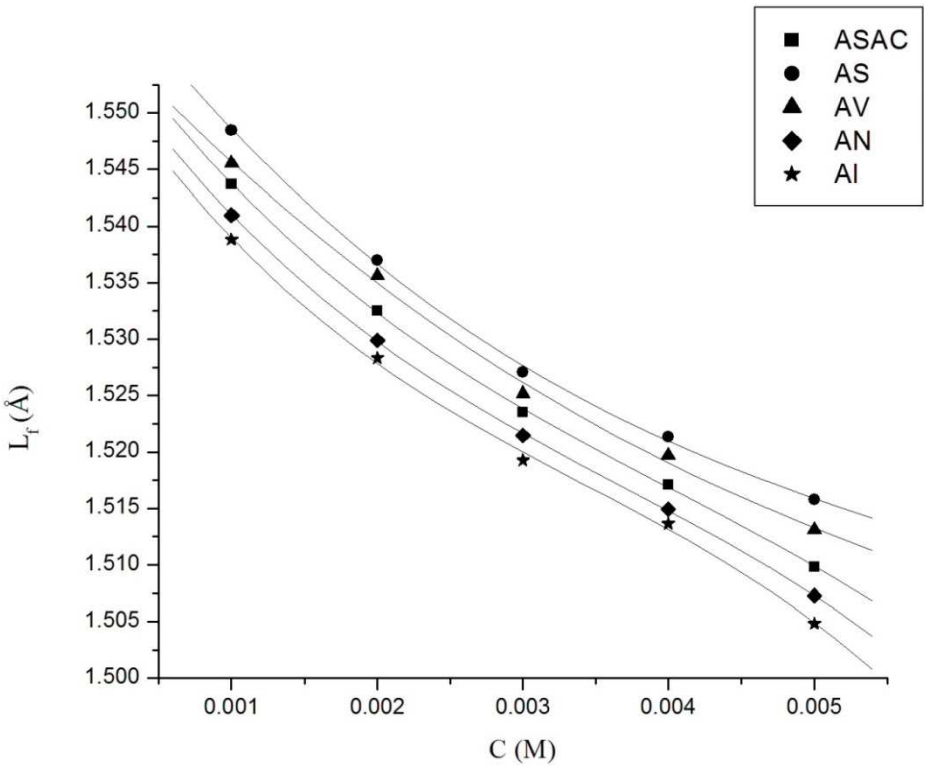


Figure 6: Variation of Intermolecular Free Length with Concentration in 70% Methanol-Water at 300.15 K.



ACKNOWLEDGEMENT
One of the author (UC) is thankful (UGC) for the award of Junior Research Fellowship. The authors are also thankful to The Head, Dept. of Chemistry, RTMNU &The Head, Dept. of Chemistry, Hislop College, Nagpur for providing laboratory facilities.

RFERENCES

[1] Amrutia, R., and Parsania, P., 2006, Ultrasonic velocity and acoustical parameters of poly(4,4-cyclohexylidenediphenyloxy-4,4-diphenylene-sulfone) solutions at different temperatures, J. Sci. Ind. Res. (65), pp. 905–911.

[2] Bhuva, B., Mehta, N., Karia, F., and Parsania, P., 2011, Effect of temperature and solvents on ultrasonic velocity and allied acoustical parameters of epoxy oleate of 9,9-bis(4-hydroxy phenyl)anthrone-10 solutions, J. Solution Chem. (40), pp. 719–726.

[3] Bell, W., and Pethrick, R.,1982, Ultrasonic investigations of linear and star shaped polybutadiene polymers in solutions of cyclohexane, and ethyl benzene, Polymer(23), pp. 369–373.

[4] Syal, V., Chauhan, A., and Chauhan, S., 2005, Ultrasonic velocity, viscosity and density studies of poly(ethylene glycols) (PEG-8,000, PEG-20,000) in acetonitrile (AN) and water (H_2O) mixtures at 25 °C, J. Pure Appl. Ultrason. (27), pp. 61–69.

[5] Iqbal, M., and Siddiquah, M.,2006, Partial molar volume of mefenamic acid in alcohol at temperature between T = 293.15 and T = 313.13 K, J. Braz. Chem. Soc. (17), pp. 851–858.

[6] Gangani, B., and Parsania, P.,2007, Microwave irradiated and classical syntheses of symmetric double Schiff bases of 1,1-bis(4-amino phenyl)cyclohexane and their physico-chemical characterization, Spectrosc. Lett. (40), pp. 97–112.

[7] Pathak, U., and Parsania, P.H., 2012, Synthesis, spectral and thermal study of novel epoxy resins based on cardosymmetric double Schiff bases, Polym. Plast. Technol. Eng. (51), pp. 75–79.

[8] Aminabhavi, T., and Patil, V., 1998, Density, viscosity, refractive index, and speed of sound in binary mixtures of ethenylbenzene with *N,N*-dimethylacetamide, tetrahydrofuran, *N,N*-dimethylformamide, 1,4-dioxane, dimethyl sulfoxide, chloroform, bromoform, and 1 chloronaphthalene in the temperature interval (298.15–308.15) K, J. Chem. Eng. Data (43), pp. 497–503.

[9] Gunasekaran, S., Natarajan R., Renganayaki, V., and Natarajan, S., 2006, Vibration spectra and thermodynamic analysis of metformin, Ind. J. Pure Appl. Phy. (44), pp. 495-500.

[10] Marzouk, S., Gaafar, M., 2007, Ultrasonic study on some borosilicate glasses doped with different transition metal oxides, Solid State Communications (144), pp. 478-483.

[11] Hartwell, S., Kehling, A., Lapanantnoppakhun, S. andGrudpan, K., 2013, Flow Injection/Sequential Injection Chromatography: A Review of Recent Developments in Low Pressure with High Performance Chemical Separation, Analytical Letters, 46(11), pp. 1640-1671.

[12] Natishan, T., 2005, Recent Developments of Achiral HPLC Methods in Pharmaceuticals Using Various Detection Modes, J. Liq. Chromatography & Related Technologies, 27(7-9), pp. 1237-1316.

[13] Vogel, A., Tatchell, A., Furnis, B., Hannaford, A., and Smith, P.,1998, Vogel's Textbook of Practical Organic Chemistry, Addison Wesley Longman, London, 5th edn., pp. 395.

[14] Pethrick, R., and Poh, B.,1983, Ultrasonic attenuation and adiabatic compressibility of polyethyleneoxide–water mixtures, Br. Polym. J. **15**, pp. 149–153.

[15] Sharma, S., Bhalodia, J., Ramani, J. and Patel, R.,2012, Volumetric, viscometricand ultrasonic study on binary mixture of oleic acid with alkyl esters at 303.15, 308.15 and 313.15 K, Int. J. Phy. Science 7(8), pp. 1205-1214.

[16] Saxena, R., and Bhatt, S., Molecular interaction in binary mixture of polymethylmethacrylate with acetic acid, Int. J. Chem. 2(2), pp. 164-172.

[17] Selvakumar, M., and Bhat, D.,2008, Molecular interaction of polymethyl methacrylate & polyethyeleneglycol solution in tetrahydrofuran, Ind. J. Pure & Appl. Phy. 46, pp. 712-718.

[18] Selvam, A.,and Geetha, D., 2008, Ultrasonic study on lamivudine: β-cyclodextrin& polymer inclusion complexes, Pakistan J. Biological Sciences 11(4), pp. 656-659.

[19] Syamala, V., Kumar, K. and Venkateswarlu, P., 2006, Volumetric, ultrasonic & viscometric study of binary mixture of DMSO with chloro & nitro substituted aromatic hydrocarbons at T=303.15 K, J. Chem. Thermodynamics 38, pp. 1553-1562.

[20] Saravanakumar, K., Baskaran, R. and Kubendran, T., 2010, Acoustic & thermodynamic properties of binary liquid mixture of acetophenone& benzene, J. Appl. Sciences 10(15), pp. 1616-1621.