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# Study of S-substituted triazinothiocarbamides in dioxane water mixture

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## ABSTRACT

In last four decades, S-triazine and thiocarbamide group containing drug create their own identity in the drug, pharmaceutical and medicinal sciences. The Viscometric Refractrometric, Interferometric measurements of recently synthesized drug have been carried out for solutions of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide  $(L_1)$  and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide  $(L_2)$  at various concentrations. Hence, density and sound velocity of biologically important substituted triazinothiocarbamides were measured at 30°C in 60% dioxane-water mixture. The result obtained during this investigation directly through light on the dipole association of compound, intermolecular attraction between solute and solvent, dielectric constant of medium, polarizability and mutual compensation of dipoles, various acoustic/ thermodynamic parameters and useful for drug absorption, transmission, stability, activity and effect of these on drugs which is base of pharmacokinetics and pharmacodynamics of any drug. Taking all these things into consideration this research work was carried out.

**Keywords:** 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide(L<sub>1</sub>), <math>1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide(L<sub>2</sub>), Interferometric measurements, Refractrometry study, Viscometric measurements.

## INTRODUCTION

In the recent era, the heterocycles and drugs are both interconnected with each other. Most of the modern drugs contain heterocyclic nucleus [1, 2]. The S-triazino compounds initiated the new branches of development in the medicinal [3,4] pharmaceutical, agricultural and biochemical fields [5-7] and used as drugs as hypoglycemic agent [3], blood pressure depressant [4] anti-tumor properties [8], anti-bacterial [2,9], anti-inflammatory [6], antipsychotic agent [7], herbicidal [10,11], insecticidal [12]. The medicinal field is undefined without heterocycles. While studying the pharmacokinetics and pharmacodynamics of these drug the viscometric measurements, refractometric measurements play an important role in medicinal and drug chemistry [13-15]. The information regarding the transport property of drugs and the ion solvent interactions can be obtained from viscometric and refractrometric measurements. These measurements provide useful information about solute-solute and solute-solvent interactions of electrolyte in binary mixtures of two liquids have been studied in terms of  $\beta$ -coefficient of viscosity [19-21].

Drug action has been widely recognized to be the ultimate consequence of physicochemical interactions between the drug and receptor. The result obtained during this investigation directly through light on the dipole association of compound, intermolecular attraction between solute and solvent, dielectric constant of medium, polarizability, and mutual compensation of dipoles and useful for transmission, stability, activity and effect of drug. The successful application of acoustic methods to physiochemical interactions of solution becomes possible after the development of adequate theoretical approaches and methods for precise ultrasonic velocity measurements in small volumes of

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liquids [12, 22-23]. Most of the information procured from ultrasonic study of fluids is confined to the determination of hydration number and compressibility [24-26]. In the basic sciences, these waves are used to provide information on the behavior of microscopic particle of matter [27]. The use of ultrasound was proved to be useful probe for generating more information on oregano metallic chemistry, biotechnology, polymerization medicinal use [28-30].

Drug receptors are the enzymes and directly hamper the drug activity and drug effects. It makes direct or indirect physical and chemical reactions with drug i.e. solute-solute interactions in the presence of solvent which changes viscosity of the phase during drug action and before testing and applying that drug to the patients, drug activity and drug effect must be evaluated. Most of the modern drugs contain heterocyclic nucleus [1,2]. S-triazino and thiocarbamido nucleus containing drugs create its own identity and significance in the medicinal, drug [31-33] and pharmaceutical chemistry [22, 34-38].

Hence for studying the potency of recently synthesized drugs in this laboratory, the viscometric measurements, refractometric measurements of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthio carbamide (L<sub>1</sub>) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide(L<sub>2</sub>) shown in **Figure 1** and **Figure 2** were studied at 30°C temperature. The result obtained during this investigation directly through light on the dipole association of compound, intermolecular attraction between solute and solvent, dielectric constant of medium, polarizability, and mutual compensation of dipoles. These results are much more useful for transmission, stability, activity and effect of drug.

#### MATERIALS AND METHODS

#### **Materials and Solutions**

Carbon dioxide free double distilled water was used. Extra pure (E. Merck) dioxane was further purified by the prescribed procedure [39] and used for preparation of ligand solutions. The entire chemical used of A.R. grade. All weighing were made on Mechaniki Zaktady Precyzying Gdansk Balance [Poland make,  $(\pm 0.001g)$ ]. The density of solutions were determined by a bicapillary Pyknometer  $(\pm 0.2\%)$  having a bulb volume of about 10 cm<sup>3</sup> and capillary having an internal diameter of 1mm and calibrated with deionised doubly distilled water. The accuracy of density measurements were within  $\pm 0.1$ Kgm<sup>-3</sup>. The viscosities were measured by means of Ostwald's viscometer thoroughly cleaned and dried. 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L<sub>1</sub>) and 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L<sub>1</sub>) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide(L<sub>2</sub>) compound are prepared by Dr. D.T. Tayade, Associate Professor, G.V.I.S.H. Amravati. India [40]. The 0.1M concentrated solution of compound these were prepared in 60% Dioxane-Water mixture. In the same way, 0.075M, 0.056M and 0.042M solutions for the compounds L were prepared. The compound used during investigations is as depicted below,







Figure 2: 1-(4-Hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide

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## **Experimental Procedure:**

The viscometer was kept in Elite thermostatic water bath and temperature variation was maintained at  $30^{\circ}$ C (±0.1) for each measurements, sufficient time was allowed to attain thermal equilibrium between viscometer and water bath. The refractive indices of solvent mixture and solutions were measured by Abbe's refractometer (±0.001). Initially, the refractometer was calibrated with glass piece (n=1.5220) provided with the instrument. For evaluating the molar refraction and polarizability constant of the compounds, we prepared 0.1M, 0.075M, 0.56M and 0.042M solutions in 60% Dioxane-Water mixture at, 30°C. The temperature was maintained by using the thermostat. The data obtained was used to compute intermolecular interactions. The Refractrometric readings were taken as described in literature [39].

Single crystal interferometer (Mittal Enterprises, Model MX-3) with accuracy  $\pm 0.03\%$  and frequency 1 MHz was used in the present work. The working of the ultrasonic interferometer was checked by measuring ultrasonic velocity of pure water at  $30^{\circ}$ C. The measured value is in good agreement [41, 42] with literature value 1510 ms<sup>-1</sup> as shown in **Table No.V.** The ultrasonic velocity was calculated for all ligands the concentration of ligands at various concentration at  $30^{\circ}$ C in 60% dioxane-water mixture. The molecular interactions were studied with solutes, the effect of these specially related to protic-aprotic nature of solvent, polarity-non polarity of solvent and hydrogen boding in solvent, dielectric constant, density, viscosity and surface tension of solvent on solute-solvent, ion-solvent and ion-ion interactions in this investigation.

### **Observations and Calculations:**

The present study deals with the viscosity, refractometric and interferrometric investigation of Ligands in 60% dioxane–water mixture at different compositions at 30°C. The readings were taken as described in literature [43]. The results obtained were mentioned in **Table I to VII**.

### **RESULTS AND DISCUSSION**

The relative viscosity of each solution during study was determined by formula depicted below

## $\eta_r = D_s \times t_s / D_\omega \times t_\omega$

Where,  $\eta_r$  = Relative viscosity of ligand solution  $D_s$  and  $D_{\omega}$ = Density of ligand solution and water  $t_s$  and  $t_{\omega}$ =Time of flow for ligand solution and water respectively

And the relative viscosities have been analyzed by Jone's-Dole equation [43]

 $(\eta_r-1)\sqrt{C}=A+\beta\sqrt{C}$ 

Where, C-is molar concentration of the ligand solution. A-is the Falkenhagen coefficient  $\beta$ -is the Jones's –Dole coefficient

Sy	stem:Ten	np 30°C	Medium - 60% Dioxane-Water						
Ligand	Conc. C (M)	√C	Time t (sec.)	Density ρx10 <sup>3</sup> (kg.cm <sup>-3</sup> )	$\eta_{r}$	η <sub>sp</sub> = η <sub>r</sub> -1	$(\eta_r-1)/\sqrt{C}$ (pa`s)		
$L_1$	0.100	0.31623	370.70	1.0236	1.5529	0.5529	1.74842		
	0.075	0.27386	357.76	1.0234	1.4984	0.4984	1.81990		
	0.056	0.23664	343.96	1.0231	1.4402	0.4402	1.86018		
	0.042	0.20494	334.12	1.0228	1.3986	0.3986	1.9b4497		
$L_2$	0.100	0.31623	392.49	1.03391	1.6607	0.6607	2.08932		
	0.075	0.27386	375.45	1.02944	1.5818	0.5818	2.12443		
	0.056	0.23664	371.80	1.02610	1.5216	0.5216	2.20416		
	0.042	0.20494	348.97	1.02180	1.4693	0.4693	2.28995		

Table No. – I - Determination of Relative and Specific Viscosities at Different Concentrations for 60% Dioxane –Water mixture.

The **Graphs 1** and **Graphs 2** are plotted between  $\sqrt{C}$  versus  $\sqrt{(\eta_r-1)}/\sqrt{C}$ . The graph for each system gave linear straight line showing validity of Jone's –Dole equation. The slope of straight line gave value of  $\beta$  coefficient.

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Graph Plotted Between  $(\eta_r - 1)/\sqrt{C}$  versus  $\sqrt{C}$  at Different Concentrations at 30°C Temperature for 60%Dioxane-Water Mixture Graph 1 - FOR L<sub>1</sub> in 60% D-W at 30°C





Table No. – II - A and β Co-Efficient Value from Graph I and Graph II at 30°C Temperatures for 60% Dioxane-Water Mixture.

Ligand	Mean "A"	β (Slope "m")
L	2.02	-1.8750
$L_2$	2.32	-1.4280

From the results in **Table I**, it is observed that, the concentration of ligand is directly proportional to density and relative viscosity for ligand L at temperature 30°C for 60% dioxane-water mixture. This may be due to the weak solvation effect which interprets weak molecule interaction. Generally, aromatic compounds have high value of relative viscosity. In this investigation, the value of relative viscosity of  $L_1$  and  $L_2$  are due to resonance stabilization in the benzene ring while S-triazino moiety which restricts the tautomeric changes in the molecule for  $L_1$  but the relative viscosity of bulkier group must be greater this may be due to the donating capacity of  $-CH_3$  group to the thiocarbamido molecule. As the thiocarbamido molecule is highly electron rich moiety and  $-CH_3$  group is also electron donating group.

The negative values of "A" and  $\beta$ -coefficient characterized as 'structure-breaker' indicating a weak solute-solvent interaction which is good for interactions in between the drug and the drug receptors shows best drug activity and drug effect and it favors pharmacokinetics and pharmacodynamics of drug. At the same time, both ligands are hydrophilic in nature and they disrupted the hydrogen bonding in the mixture of solvent causing lesser molecular interaction. Thus these factors plays important role during designing of any drug. The value of A coefficient show that, the solute-solvent interaction is highest among the molecules of ligand L<sub>1</sub> at 30°C for 60% Dioxane-water mixture and so they tend to interact with solvent molecules to lesser extent leading decrease in solute-solvent interaction. From this discussion , it is clear that bulky substituent on the molecule is not only factor in trend of relative viscosity but the reactivity and stability and tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in ligands and the compactness in the molecule will directly hampered results and trends in the relative viscosity.

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The molar refraction of solutions of compound in Dioxane-Water mixture were determined by a following equation,

$$\mathbf{R}_{\text{mixture}} = [(\hat{\eta}^2 \cdot 1)/(\hat{\eta}^2 + 2)] \{ [X_1 M_1 + X_2 M_2 + X_3 M_3]/d \}$$

Where,

 $\dot{\eta}$  is the refractive index of solution, X<sub>1</sub> is mole function of Dioxane, X<sub>2</sub> is mole function of Water, X<sub>3</sub> is mole function of Solute, M<sub>1</sub>, M<sub>2</sub>, M<sub>3</sub> are molecular weights of Dioxane, water and solute respectively, D is density of solution

The molar refraction of compound is calculated as,

### $\mathbf{R}_{\text{lig}} = \mathbf{R}_{\text{mixture}} - \mathbf{R}_{\text{Dioxane-Water}}$

## Where,

 $R_{\text{Dioxane-Water}}$  - The molar refraction of solvent, Dioxane-Water mixture.

The polarizability constant ( $\alpha$ ) of compound is calculated from the following relation,

 $R_{lig} = (4/3) \pi \text{ No } \alpha$ 

Where, No is Avogadro's number.

#### Table No. - III- Molar Refraction of Different Percentage of Dioxane - Water Mixture

% Dioxane-Water Mixture	Molar Refraction (RM) (cm <sup>3</sup> . Mole <sup>-1</sup> )
100	21.5977
90	15.4584
80	11.9390
70	9.6554
60	8.0551

Table No. - IV - Determination of Molar Refraction and Polarizability Constant at Different Concentrations for 60% of Dioxane-Water Mixture

Ligand	Concentration (M)	Density ρx10 <sup>3</sup> (kg.cm <sup>-</sup>	Refractive Index η	R <sub>mix</sub> (cm <sup>3</sup> .mole <sup>-1)</sup>	R <sub>Ligand</sub> (cm <sup>3</sup> .mole <sup>-1</sup> )	αx10 <sup>-23</sup> (cm <sup>3</sup> )
	0.1000	1.0236	1.4102	8.8427	0.7876	0.03121
$L_1$	0.0750	1.0234	1.4082	8.7597	0.7046	0.02796
	0.0560	1.0231	1.4070	8.7029	0.6478	0.02567
	0.0420	1.0228	1.4052	8.6385	0.5834	0.02312
$L_2$	0.1000	1.0339	1.4088	8.4877	0.4326	0.01715
	0.0750	1.0294	1.4076	8.4690	0.4139	0.01640
	0.0560	1.0261	1.4062	8.4442	0.3891	0.01542
	0.0420	1.0218	1.4048	8.4301	0.3750	0.01486

The values of molar refraction of Dioxane in 60% Dioxane-Water mixture are presented in **Table III**. The values of molar refraction and polarizability constant of compound L in 60% of Dioxane-Water mixture are presented in **Table III and IV**.

Graph Plotted Between Refractive Index ( $\eta$ ) Versus C at Different Concentrations at 30°C Temperature for 60%, Dioxane-Water Mixture.



Graph 3 - FOR L<sub>1</sub> in 60% D-W at 30°C

Graph 4 - FOR L<sub>2</sub> in 60% D-W at 30°C



From the **Graph 3 and 4**, it can be predicted that, at 30°C the temperature of mixture, the molar refractivity (true molar volume) continuously increases with concentration. At the same time, the polarizability constant of compound ( $\alpha$ ) also increases. This may be attributed to the fact that at this temperature of dioxane, there is increase in dielectric constant of medium with concentration and also considerable dipole association (intermolecular attraction) take place, which would be accompanied by increases in polarizability. It is observed from **Table III and IV**. When there is bulkier group, the molar refraction is greater. But in this investigation the value of molar refraction of compound L was high. It was observed that only the bulkiness of the group as a substituent was not only interfere the values of molar refraction but also the reactivity and stability, tautomeric properties also interfere the values of molar refraction. It was clear from the result that in L there was resonance stabilization in benzene ring which was substituted on one nitrogen of thiocarbamide at the same time on nitrogen of the same molecule; there was S-triazino moiety which restricts the tautomeric changes in L molecule.

An addition of polar solute having a partial positive charge on hydrogen atom, there is every likely hood that there can be a weak interactions between this positive charge and negative charge on oxygen atom (due to electro negativity) of dioxane. This weak interaction of the wonder wall's forces is expected to introduce the structuredness in the solution i.e. specific arrangement of dioxane molecule may be occurring due to attached solute molecule. Thus, spaces may be created making the solution more compressible as it appears from the higher apparent molar compressibility value in dioxane solvent.

Sr. No.	No. of Rotation of Screw	Micrometer Reading (mm)	Difference Between Reading (mm)	Distance Travelled By Screw in One Rotation	Average Ultrasonic Velocity (m/sec)
1	5	26.7843	3.7654	1.50616	
2	10	23.0189	3.7584	1.50336	
3	15	19.2605	3.7544	1.50176	
4	20	15.5061	3.7002	1.48008	1501 2014
5	25	11.8059	3.7468	1.49872	1301.2914
6	30	8.0591	3.7583	1.50332	
7	35	4.3008	3.7891	1.51564	
8	40	0.5117		10.50904	

Table No v - Average Ultrasonic velocity of water at 50 C	Table No V	- Average	Ultrasonic	Velocity of	Water at 30°C
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D- W %	Sr. No.	No. of Rotation of Screw	Micrometer Reading (mm)	Difference Between Reading	Distance Travelled By Screw in One Rotation	Average Ultrasonic Velocity (v <sub>0</sub> ) (m/sec)	Density (d <sub>0</sub> ) (Kg.m <sup>-</sup> <sup>3</sup> )	$\begin{array}{c} \beta_0 \underset{10}{x} 10^{-} \\ (Pa^{-1}) \end{array}$
	1	5	20.0328	3.7055	1.4822		1026.2	4.4625
60	2	10	16.3273	3.7255	1.4902	1477.72		
	3	15	12.6018	3.6907	1.4763			
	4	20	8.9111	3.6555	1.4622	14//./2		
	5	25	5.2556					
					5.9109			

Ligand	Conc. C (Mole/lit)	Average Ultrasonic Velocity V (m/sec )	Density d <sub>s</sub> (Kg.m <sup>-3</sup> )	βsx10 <sup>-10</sup> (pa <sup>-1</sup> )	<b>\$</b> v (m <sup>3</sup> mol <sup>-1</sup> )	φ <sub>k</sub> x10 <sup>-10</sup>	L <sub>f</sub> (A <sub>0</sub> )	RA	Z * 10 <sup>4</sup> (Kgm <sup>-2</sup> sec <sup>-1</sup> )
$\mathbf{L}_{1}$	0.1	1683.89	1023.6	3.4454	0.2797	-8.9475	0.0117	0.9550	172.3630
	0.075	1582.9	1023.4	3.8998	0.2817	-6.1779	0.0125	0.9747	161.9940
	0.056	1434.675	1023.1	4.7487	0.2846	6.4420	0.0138	1.0069	146.7816
	0.042	1286.695	1022.8	5.9055	0.2876	35.4424	0.0153	1.0438	131.6032
$L_2$	0.1	1583.89	1033.9	3.8554	0.1799	-5.4015	0.0124	0.9845	163.7584
	0.075	1421.975	1029.4	4.8043	0.2233	5.2410	0.0138	1.0161	146.3781
	0.056	1278.675	1026.1	5.9606	0.2085	27.3144	0.0154	1.0493	131.2048
	0.042	1130.175	1021.8	7.6620	0.2504	76.5963	0.0175	1.0888	115.4813

Plot Between Apparent molar volume  $(\varphi_v)$  Vs concentration  $(\sqrt{C})$  for Ligand L at 30°C for 60% dioxane-water mixture

Graph 5- L1 at 30°C for \$\$\phi\_v\$



## Graph 6- $L_2$ at 30°C for $\phi_v$



Plot between Apparent molar compressibility  $(\phi_k)$  Vs concentration  $(\sqrt{C})$  for Ligand L at 30°C for 60% dioxane-water mixture



Graph 7 –  $L_1$  at 30 °C for  $\phi_K$ 



The adiabatic compressibility shows the increase association of molecules by lower  $\beta$  value.

$$\beta = 1/Vs2d$$

 $\phi_{K} = [1000 (\beta_{s}d_{0} - \beta_{0}d_{s}) / md_{s}d_{0}] + ((\beta_{s} M/d_{s}))$ 

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Where,

M = molecular weight of solute  $\beta_0$  = adiabatic compressibility of pure solvent and  $\beta_s$  = adiabatic compressibility of solution

 $d_0$  = density of pure solvent

 $d_s = density of solution$ m = molality of solution

Whereas, apparent molar compressibility also shows in Table No V to VII. The increase association but at the same time the structuredness of the solution by higher  $\phi_{\rm K}$  values. It is also observed from the graphs that positive values of  $\phi_{\rm K}$  for ligands indicates electro static force in the vicinity of ions [44, 45].

## $\phi_{\rm V} = [1000(d_0 - d_s) / md_0 d_s] + (M/d_s)$

From the difference in trends in two compressibility's, adiabatic & apparent molar, it may be predicted that adiabatic

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compressibility can detect gross changes in interactions but minute changes due to change in structure may only be noticed by apparent molar compressibility( $\phi_K$ ). Thus, the structure of solute and the number of atoms present in it will have direct effect on  $\phi_{K}$  value. The parameters of solvents which directly affect the values of  $\beta$  are high density of dioxane as compare to protic nature, polarity, high dielectric constant (24.6).

Similarly on increasing the concentration of ligands,  $\beta$  decreases continuously. The increased concentration of solute will require more and more number of solvent molecules to dissolve it resulting in breaking the electrostriction/ structuredness of solvent consequently decreasing the compressibility. Thus in both the system solute-solvent and solvent-solvent interactions are involved which are reflected in the compressibility values.

The conventional approach based on compressibility is both useful and fundamental, in fact it constitutes an additional probe for studying molecular interactions. The Graph 3 and 4 satisfy this thought and specific acoustic impedance is the complex ration of the effective sound pressure at a point to the effective particle velocity at that point<sup>46</sup>.

In case of dioxane, because of its non-polar nature, the compact packing of molecules is already there and when polar solute is added because of its association again free space decreases. Therefore, the  $L_{\rm f}$  values in dioxane must be smaller. When the metal ions are added, the polar-polar associations still increases and the L<sub>f</sub> decreases Ultrasonic velocity depends upon intermolecular free length  $L_f$  with decrease in free length velocity increases or vice versa.

$$L_{\rm f} = K. (\beta_{\rm s})^{1/2}$$

Where,  $L_f =$  Intermolecular Free Length K = Jacobson's constant

Relative association  $R_A$  is an acoustic property of understanding interaction, which is influenced by two opposing factors.

$$R_{A} = d_{s} / d_{0} [V_{0}/V_{S}]^{1/3}$$

$$Z = V_{s} d_{s}$$
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 $\mathbf{Z} = \mathbf{V}_{\mathbf{s}} \mathbf{d}_{\mathbf{s}}$ 

Where,  $V_0 =$  Ultrasonic velocities in a solvent  $V_s$  = Ultrasonic velocity of solution

• Breaking of solvent structure on addition of solute to it satisfies decreases in values when concentration of ligand L in 60% dioxane-water mixture increases with temperature increase. It was observed that, the value of  $R_A$  of ligand L gets affected by the resonance stabilization in benzene.

• Solvation of solute that is simultaneously present by the free solvent molecules. It was clearly observed that the high concentration of solute. The values of  $R_A$  at high percentage of dioxane are very well explained by second factor.

In the present work, non specific solute-solvent association caused by the dielectric enrichment in the solvent shell of solute takes place resulting weak molecular interaction. The presence of weak solute-solvent interaction may be due to strong hydrogen bonding is present and in a dilute solution, solute molecules can disrupt this H-bonding to lesser extent. These factors may directly interfere the solute-solvent interaction. Measurement of ultrasonic velocity is the best tool to investigate solute-solvent, solute-solute and ion-solvent interactions. Therefore, in last four decades ultrasonic interferometric study created its own identity for determining solute-solvent interactions. By this study  $\beta$ ,  $\phi_{x}$ ,  $\phi_{K}$ ,  $L_{f}$ ,  $R_{A}$ , Z, etc. acoustic properties were determined which explain how these interactions occur and responsible for breaking and making of the structure in the solution. So in the present work these acoustic parameters were studied for newly synthesized ligands, which were used as solutes. In general it is observed that, all these values of ligand L clearly indicate effects of resonance stabilization in benzene ring which is a substituent on thiocarbamido nucleus. At the same time bulkier nature of phenyl group may also interfere during these interactions. This clearly indicates that not only the bulkier nature and nature of ligand will affect but the molecular weight of solute is also one of an important factor which directly affects the solute-solvent interaction. The change in values of  $L_{\rm f}$  may be due to stronger interaction between ions and solvent molecules at that particular percentage combination of dioxane-water mixture decrease in  $L_f$  values indicated weaker interaction between ions and solvent molecules. The intermolecular free length goes on decreasing with increase in concentration of solute indicates decrease in free space between the molecules because of stronger solute-solvent interaction which is in a agreement with on observed value of  $\beta$ . From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds is more effective at this concentration of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamides.

To study the pharmacokinetics and pharmacodynamics of any drug relating these ligands, the acoustic parameters of dioxane helps to find out the property of solvent interfere in breaking and making of structure of solvent. From this study it is clear that properties, which are directly or indirectly responsible for these are protic-aprotic nature of solvents, dielectric constant, polarity, density, tendency of forming hydrogen bonding, surface tension, viscosity of solvent, bulkier nature, resonance, reactivity of group, size and molecular weight of ligand.

## CONCLUSION

Hence from all three method, it was clear that bulky substituent on the molecule was not only factor in trend but tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in compounds and compactness in the molecule will directly hampered results and trends. It means that in 60% of dioxane, the solute-solvent interactions i.e. interaction of compounds (drugs) and dioxane is more but phenyl substituted drug shows more reactivity as compare to methyl substituent, which may affect the drug activity. By every method it is proved. So we can cross verify the reactivity of our ligand by these techniques.

From this study it can be concluded that interferometric technique requires minimum efforts, solutions and is somewhat a direct method as compare to other two and has its own identity and significance in material sciences, which can give idea about effectiveness of solvent. By knowing these parameters the selection of solvent during synthesis in organic and coordination chemistry can be predicted. This study is an important basic tool for pharmaceutical, medicinal and biochemical sciences which directly focus on drug activity and drug effect at primary level and then onwards only the characteristics of drug can be decided. This study gave detail information regarding pharmacokinetics and pharmacodynamics of drug.

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