Interferometric study of s-substituted Triazinothiocarbamides in 70% Dioxane water mixture

Tayade DT¹, Kshirsagar AM²

1. Associate Professor, Dept. of Chemistry, Govt. Institute of Science and Humanities, S.G.B. Amravati University, Amravati (M.S.), India
2. Assistant Professor, Dept. of Chemistry, Alamur Rahamala Institute of Engineering & Technology, Mumbai University, Mumbai (M.S.), India

Corresponding author: Research scholar, S.G.B. Amravati University, Amravati (M.S.), India, Mail: ashwinkshirsagar2@gmail.com, Mobile No: (+91)9545192107

Received 09 May; accepted 14 June; published online 01 July; printed 16 July 2013

ABSTRACT

S-triazine and thiocarbamide group containing drug create their own identity in the drug, pharmaceutical and medicinal sciences in last four decades. Hence, density and sound velocity of some biologically important substituted triazinothiocarbamides were measured at 30°C in 70% dioxane-water mixture. The interferometric measurements of recently synthesized drugs have been carried out for solutions of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L₁), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide (L₂) and 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L₃) at various concentrations. This data have been used to determine various acoustic / thermodynamic parameters. These properties are used to interpret weak molecular solute-solvent, solute-solute interactions in the system. The data and result obtained during this investigation gave detail information regarding drug absorption, transmission, activity and effect of these 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-substitutedthiocarbamides, dioxane-water mixture, interferometric measurements, pharmacokinetics, pharmacodynamics.

1. INTRODUCTION

Most of the modern drugs contain heterocyclic nucleus (Solanki et al. 2007, Yakaiah et al. 2007). The S-triazine compounds initiated the new branches of development in the medicinal (Nitha et al. 2010, Yang et al. 2010), pharmaceutical (Krauth et al. 2010), agricultural (Gang et al. 2005) and biochemical fields (Srinivas et al. 2006, Adebiyi et al. 2009, Frankenberg et al. 2008). 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 liquids (Jain et al. 2007, Garcia et al. 2008, Piletska et al. 2005). Most of the information procured from ultrasonic study of fluids is confined to the determination of dielectric constant of medium, polarizability, and mutual compensation of dipoles and useful for transmission, stability, activity and effect of drug. Hence for studying the potency of recently synthesized drugs in G.I.S.H, Amravati laboratory in the month of May 2012, the interferometric measurements of 1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide (L₁), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide (L₂), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L₃) were studied in 80% dioxane water mixture. S-triazino and thiocarbamido nucleus containing drugs create its own identity and significance in drug, pharmaceutical and agricultural chemistry (Pakar 1982, Meshram et al. 2010, Annappan and Palani 2007, Hernandez et al. 2008, Baldaniya and Patel 2009, Solankie et al. 2009, Burke et al. 1982, Chand e et al. 1998).

2. SCOPE OF THE STUDY

The aim of carrying out this research is to study the drug suitability by studying the solute solvent interaction by viscometric, refractometric and interferometric methods by cross verifying their results in common dioxane medium. So the pharmacokinetic and pharmacodynamics study become easy in medicinal chemistry.

2.1 Materials

1-(4-Hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamide(L₁), 1-(4-hydroxy-6-methyl)-S-triazino-3-ethylthiocarbamide (L₂), 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L₃) were synthesized which were used as ligand (Vogel (1974)). The general structures of substituted thiocarbamides as shown in Figure-a, Figure-b and Figure-c. All the solutions of ligand were prepared fresh in the present investigation.
2.2. Methods

Carbon dioxide free double distilled water was used. Extra pure (E. Merck) dioxane was further purified by the prescribed procedure (Vogel 1974) and used for preparation of ligand solutions. The densities of the solutions were determined by a bicipillary Pyknometer (±0.2%). Weighing was made on electronic balance, made by Mechaniki Zaktydy Precyzyjnej Gdansk Balance, made in Poland (±0.001 gm). A special thermostatic arrangement was done for density. Single crystal interferometer (Mittal Enterprises, Model MX-3) with accuracy ±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°C. The measured value is in good agreement (Pandey et al. 1987, Ali and Shahajahan 2006) with literature value 1510 check value ms⁻¹. The ultrasonic velocity was calculated for all three ligands the concentration of ligands at various concentration at 30°C in 70% 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 bonding in solvent, dielectric constant, density, viscosity and surface tension of solvent on solute-solvent, ion-solvent and ion-ion interactions in this investigation.

3. OBSERVATIONS AND CALCULATIONS

The present study deals with the interferometric investigation of Ligand (L) in 70% dioxane-water mixture at different compositions at 30°C. The readings were taken as described in literature. The results obtained were mentioned in Table 1-3.

4. RESULTS

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. An addition of polar solute having a partial positive charge on hydrogen atom, there is every likelihood 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. The adiabatic compressibility shows the increase association of molecules by lower β value.

\[ \beta = 1/V_s^2d \]

Where, 
\[ \beta = \text{adiabatic compressibility of pure solvent} \]
\[ \beta = \text{adiabatic compressibility of solution} \]

\[ V_s = \text{ultrasonic velocities in a solvent} \]
\[ V_u = \text{ultrasonic velocity of solution} \]

M = molecular weight of solute
\[ \beta_s = \text{adiabatic compressibility of pure solvent} \]
\[ \beta_s = \text{adiabatic compressibility of solution} \]

Whereas, apparent molar compressibility also shows the increase association but at the same time the structuredness of the solution by higher \( \psi \) values. It is confirmed by Graph (d), Graph (e), Graph (f) for ligand L₁, L₂, L₃. It is also observed that positive values of \( \psi \) for ligands indicates electro static force in the vicinity of ions (Masson 1929, Aswale et al. 2012). 

From the difference in trends in two compressibility’s, adiabatic & apparent molar, it may be predicted that adiabatic compressibility can detect gross changes in interactions but minute changes due to change in structure may only be noticed by apparent molar compressibility(\( \psi \)). Thus, the structure of solute and the number of atoms present in it will have direct effect on \( \psi \) 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. Specific acoustic impedance is the complex ration of the effective sound pressure at a point to the effective particle velocity at that point (Burke et al. 1982). 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 L₁ values in dioxane must be smaller. When the metal ions are added, the polar-polar associations still increases and the L₁ decreases Ultrasonic velocity depends upon intermolecular free length L₁ with decrease in free length velocity increases or vice versa. 

\[ L_1 = K, \beta_s^{1/2} \]

Where, 
\[ L_1 = \text{Intermolecular Free Length} \]
\[ K = \text{Jacobson’s constant} \]

Relative association \( R_a \) is an acoustic property of understanding interaction, which is influenced by two opposing factors, 

\[ R_a = d_s/d_h (V_u/V_s)^{1/3} \]

Where,
\[ V_u = \text{ultrasonic velocities in a solvent} \]
\[ V_s = \text{ultrasonic velocity of solution} \]

Breakings of solvation structure on addition of solute to it satisfy decreases in values when concentration of ligand in 70% 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.
Interferometric study of s-substituted Triazinohiocarbamides in 70% Dioxane water mixture, Discovery Sci., 2013, 5(13), 7-12, www.discovery.org.in/ds.htm

4. DISCUSSION

In this investigation, in L1 there is resonance stabilization in the benzene ring while S-triazino moiety which restrict the tautomeric changes in the molecule. But when we compare, the values of L1 and L2, the bulkier group must be greater this may be due to the donating capacity of –CH3 group to the thio carbamido molecule. As the thio carbamido molecule is highly electron rich moiety and –CH3 group is also electron donating group, hence in L2 molecule there occur compactness in the bond which is greater than L1 molecule. From this discussion, it is clear that bulky substituent on the molecule is not only factor in trend of acoustic parameters 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 acoustic parameters.

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 β, ϕ1, ϕc, L1, R, 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. 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. All these parameters play important role in pharmaceutical and medicinal drug chemistry. From this study it can be concluded that interferometric technique requires minimum efforts, solutions and is somewhat a direct method and has its own identity.

Tayade et al.
Interferometric study of s-substituted Triazinothiocarbamides in 70% Dioxane water mixture, Discovery Sci., 2013, 5(13), 7-12, www.discovery.org.in/ds.htm
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.

5. CONCLUSION
As at high percentages of dioxane in dioxane-water system indicate the pronic nature, polarity, dielectric constant and tendency of formation of hydrogen bonding in solvent in the system decreases. Hence, it may cause decreases values of β for L1, L2, L3. Hence from the above discussion, 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 when the high percentage of dioxane in the solute-solvent interactions i.e. interaction of compounds (drugs) and dioxane which may be stabilize the drug activity. From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds L1, L2, L3 is effective at high concentration of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamidates.

SUMMARY OF RESEARCH
1. Detail study by interferometric methods and determine various acoustic thermodynamic parameters to interpret weak molecular solute-solvent, solute-solute interactions in the system.
2. The result obtained during this investigation gave detail information regarding drug absorption, transmission, activity and effect of these drugs which is base of pharmacokinetics and pharmacodynamics of any drug.
3. These compounds are suitable at lower concentration and 30°C temperature in 70% dioxane-water medium.
4. These thiocarbamides plays important role in drug synthesis and drug designing process in pharmaceutical field because of its tautomeric stability.

FUTURE ISSUES
From the finding, study of thiocarbamido drug in dioxane medium get easy and it make easy study of these drug with their basic parameters which will be useful for pharmaceutical industry.

DISCLOSURE STATEMENT
There is no financial support for this research work from the funding agency.

ACKNOWLEDGMENT
I am very thankful to Dr. D. T. Tayade for checking & giving valuable suggestions in my research papers.

REFERENCES