

**“EFFECT OF TEMPERATURE ON REFRACTOMETRIC STUDY OF  
TRIZINOTHIOCARBAMIDES IN 70% DIOXANE-WATER MIXTURE”**

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**Abstract:**

The pharmaceutical and medicinal applications of the synthesized drugs, it is a prior duty of chemist to investigate pharmacokinetic and pharmacodynamics of that drug for studying drug absorption, transmission metabolism and drug excretion, hence it become essential to investigate the solute-solvent, solvent-solvent and solute-solute-solvent interactions of that drug. (Here solute means drug) These interactions were directly hamper the potency of that drug as well as the drug activity and effect. This study explores the potency of newly synthesized drugs, stability of drug and also to renovate and modify the traditional drugs which are used by medicinal practioners. S-triazine and thiocarbamide group containing drug create their own identity in pharmaceutical and medicinal sciences. Refractometric measurements of recently synthesized drugs viz. 1-(4-hydroxy-6-methyl)-S-triazino-3-methylthiocarbamide (L<sub>1</sub>) is carried out at 70% percentage composition of solvent and at different temperatures to investigate effects of structure, groups on S-triazino thiocarbamides. The data and the results obtained during this investigation gave detail information regarding drug absorption, transmissions activity and effect of these drugs. Taking all these things in to consideration this research work was carried out.

**Keywords:**

1-(4-hydroxy-6-methyl)-S-triazino-3-phenylthiocarbamides, Dioxane-Water mixture, Refractometry study.

**1. Introduction**

Pharmaceutical, medicinal and biochemical literature survey reveals that S-triazino and thiocarbamido nucleus containing drugs have their own identity in drug chemistry. One of a unique and important property of liquid is refractive index. When a ray of light passes from less dense to denser medium then there is a change in the direction of refraction and also angle of refraction changes and ultimately the refractive index changed. The result obtained during this investigation directly through light on the dipole association of ligand, 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 hence this study is essential. Many of them are used as drugs as muscle relaxant<sup>1</sup>, hypoglycemic agent<sup>2</sup>, blood pressure depressant<sup>3</sup>, anti-diabetic drug<sup>4</sup>. With the development in medical field, it is reported that the drug having S-triazino nucleus possess anti-tumor properties<sup>5-6</sup>, anti-bacterial<sup>7-9</sup>, anti-inflammetry<sup>10</sup> and anti-cancer properties<sup>11-13</sup>. Results of refractometric measurements directly gave information regarding solute-solvent,

solvent-solvent interactions. Taking all these things into consideration the present investigation was carried out in various percentage compositions and at different temperatures. This is hitherto unknown. This study becomes a milestone in the drug, medicinal, pharmaceutical of triazinothiocarbamido molecules.

### 1.1 Experimental

All weighings were made on Mechaniki Zaktady Precyzying Gdansk Balance [Poland make, ( $\pm 0.001\text{g}$ )]. The densities of solutions were determined by a bicapillary Pyknometer ( $\pm 0.2\%$ ) having a bulb volume of about  $10\text{cm}^3$  and capillary having an internal diameter of 1mm. The 0.1M solution of ligand was prepared in 60%, 70% and 80% dioxane-water mixture and the solutions of different concentrations of ligands in 60%, 70% and 80% dioxane-water mixture were prepared. The refractive indices of solvent mixture and solutions were measured by Abbe's refractometer ( $\pm 0.001$ ) at different concentrations and various temperatures. The temperature of the prism box was maintained at  $27^\circ\text{C}$ . Initially, the refractometer was calibrated with a glass piece ( $n=1.5220$ ) provided with the instrument.

### 1.2 Observation and Calculation

The present work deals with the study of molar refraction and polarizability constant of ligand 70% dioxane-water mixtures at different compositions. The data obtained have been used to compute intermolecular interactions. The refractometric readings were taken as described in literature.

<b>% of Dioxane-Water Mixture</b>	<b>Molar Refraction (RM) (<math>\text{cm}^3 \cdot \text{Mole}^{-1}</math>)</b>
100	21.5977
90	15.4584
80	11.9390
70	9.6554
60	8.0551

Temp ( $^\circ\text{C}$ )	Concentration (M)	Density $\rho \times 10^3$	Refractive Index	$R_{\text{mix}}$ ( $\text{cm}^3 \cdot \text{mole}^{-1}$ )	$R_{\text{Ligand}}$ ( $\text{cm}^3 \cdot \text{mole}^{-1}$ )	$\alpha \times 10^{-23}$ ( $\text{cm}^3$ )
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		(kg.cm-3)	$\eta$			
20	0.1000	1.0394	1.4138	10.0514	0.3950	0.01565
	0.0750	1.0324	1.4122	10.0490	0.3926	0.01556
	0.0560	1.0293	1.4110	10.0230	0.3666	0.01453
	0.0420	1.0261	1.4098	10.0078	0.3514	0.01392
30	0.1000	1.0387	1.4122	10.0244	0.3680	0.01458
	0.0750	1.0334	1.4112	10.0178	0.3614	0.01432
	0.0560	1.0290	1.4104	10.0130	0.3566	0.01413
	0.0420	1.0257	1.4088	9.9902	0.3338	0.01323
40	0.1000	1.0378	1.4114	10.0155	0.3591	0.01423
	0.0750	1.0326	1.4102	10.0041	0.3477	0.01378
	0.0560	1.0294	1.4090	9.9791	0.3227	0.01279
	0.0420	1.0251	1.4072	9.9615	0.3051	0.01209

Graph Plotted Between Refractive Index ( $\eta$ ) Versus C at Different Concentrations and Temperature for 70% Dioxane-Water Mixture.

Fig.3: Fig.4: FOR  $L_1$  in 70% D-W at 20°C

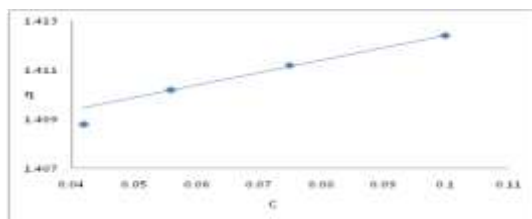


Fig.5: FOR  $L_1$  in 70% D-W at 30°C

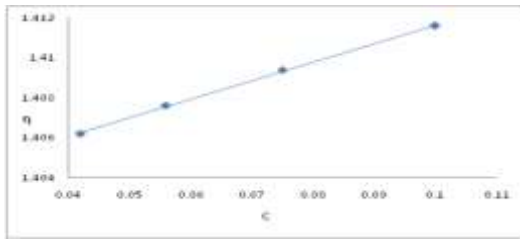


Fig.6: FOR  $L_1$  in 70% D-W at 40°C

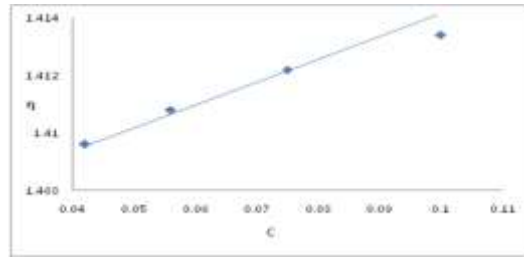
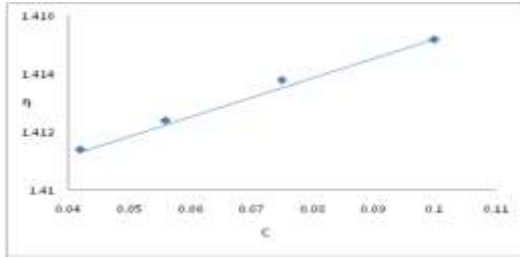
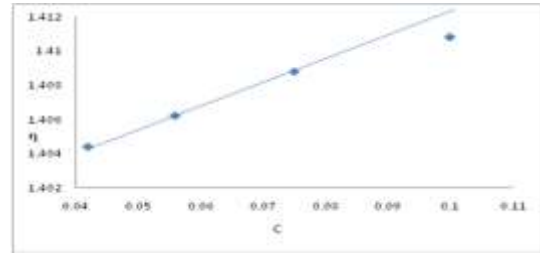
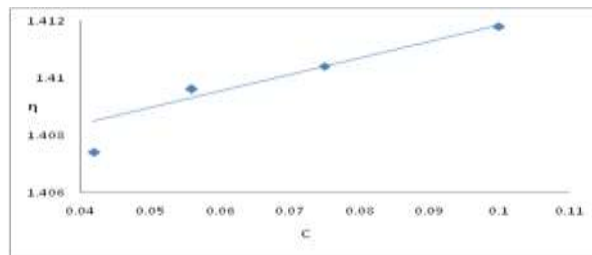


Fig.9: FOR  $L_1$  in 80% D-W at 40°C



## 2. Result and Discussion

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

$$R_{\text{mixture}} = [(\eta^2 - 1) / (\eta^2 + 2)] \{ [X_1 M_1 + X_2 M_2 + X_3 M_3] / d \} \quad \text{-----①}$$

Where,

$\eta$  is the refractive index of solution,

$X_1$  is mole function of Dioxane,

$X_2$  is mole function of Water,

$X_3$  is mole function of Solute,

$M_1, M_2, M_3$  are molecular weights of Dioxane, water and solute respectively,

$D$  is density of solution

The molar refraction of ligand is calculated as,

$$R_{\text{lig}} = R_{\text{mixture}} - R_{\text{Dioxane-Water}} \quad \text{-----②}$$

Where,

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

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

$$R_{\text{lig}} = (4/3) \pi N_0 \alpha \quad \text{-----} \textcircled{3}$$

Where,  $N_0$  is Avogadro's number.

The values of molar refraction of Dioxane-Water mixture were presented in Table No I. The values of molar refraction and polarizability constant of ligand in 60%, 70% and 80% of Dioxane-Water mixtures were presented in Table No. II to IV. From the results, it is observed that, the concentration of ligand is directly proportional to density and refractive index for ligand at temperature 20°C, 30°C and 40°C. This may be due to the weak solvation effect which interprets weak molecule interaction. The 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, ligand is 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.

From the table, it is observed that, the temperature of solution is inversely proportional to the density and refractive index for ligand at all concentration. It is due to the temperature increase, randomness of solute molecule in solution also increases shows weak the molecular interactions. From this discussion, it is clear that substituent on the molecule is not only factor in trend of refractive index but the reactivity and stability and tautomeric conversion as well as electron donating nature, electron clouds, nature of hetero atom present in ligand and the compactness in the molecule will directly hampered results and trends in the refractive index.

It shows that, the molar refractivity (true molar volume) as well as the polarizability constant of ligand may be attributed to the fact that, the dipole in the ligand lies perpendicular to the longer axis of the molecules and in the presence of dioxane causing decrease in dielectric constant of medium, considerable dipole association (intermolecular attraction) take place which would be accompanied by decreases in polarizability as well as molar refractivity because of the mutual compensation of dipoles. In the present work, non specific solute-solvent association caused by the dielectric enrichment in the solvent shell of solute takes place result may be due to strong hydrogen bonding resulting weak molecular interaction and in a dilute solution, solute molecules can disrupt this H-bonding to lesser extent.

The results obtain in refractometric study directly shows merits or demerits of that drug. The literature survey also shows that the transport of drug which is a part of pharmacokinetics which involved drugs absorption, drug distribution (transmission), drug metabolism and drug excretion in which solute-solvent interactions were studied. While in pharmacodynamics drug and drug interactions (solute-solvent interactions) were studied. Drug transport and drug receptor interactions were studied in pharmacokinetics and pharmacodynamics respectively. Pharmacokinetics and pharmacodynamics parameters can also be determined by refractometric study. Interpretation of nature of chemical reactions involved in pharmacodynamics and pharmacokinetics can be easily predicted by obtaining results of refractometric measurements as drug and drug receptor interactions is also depends upon refractive index<sup>14-16</sup> and transport of drug<sup>17-20</sup> also depends upon this factor. Hence, refractometric study creates its own importance and identify in the medicinal, pharmaceuticals, biochemical and chemical sciences. So it become prior duty of chemist before giving final result and opinion about any drug, the result must be cross verified and then only result must be determined. Taking all these things into consideration, the molar refraction and polarizability constant of ligand 1-(4-hydroxy-6-methyl)-S-triazino--phenylthiocarbamide  $L_1$  was studied in various percentage of dioxane-water mixture at different and also at various concentrations and temperature.

## 2.1 Conclusion:

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 in the molar refraction. It means that when the temperature of dioxane increases, weak solute-solvent interactions i.e. interaction of compounds (drugs) and dioxane increases, which may be stabilize the drug activity. From this it can be concluded that the drug absorption, drug transmission and drug effect of compounds is more effective at higher temperature of dioxane. This study may become a milestone in the drug, medicinal and pharmaceutical chemistry of triazino thiocarbamides.

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