REFRACTOMETRIC STUDY OF NOVEL BENZOTHIAZOLYL AND BENZIMIDAZOLYL SUBSTITUTED DERIVATIVE IN BINARY LIQUID MIXTURE

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Abstract: Refractive indices of novel benzothiazolyl and benzimidazolyl substituted derivatives in different percentage of binary liquid mixture at 30 ± 0.1 ˚C were measured by Abbe's refractrometer. The data obtained was used to calculate polarizability constant and molar refraction which explain solute-solvent interactions.

Index Terms: **Refractive indices, molar refraction, molecular interaction.**

INTRODUCTION:

One of the unique and important properties of fluid is the refractive index. When a ray of light travels from less dense to more dense medium, there is a change in the direction of refraction as well as changes in the angle of refraction and the refractive index has finally changed. During this investigation, the result was obtained directly by light on the ligand dipole association, intermolecular attraction between solvent and solute, medium dielectric constant, polarizabililty and dipole mutual compensation of dipole. These results are much more useful for the drug's transmission, stability, activity and effect, so this study is important. In the present study, pharmaceutical, medicinal and biochemical literature survey reveals that Benzothiazole derivatives are widely found in bioorganic and medicinal chemistry with drug discovery and autoimmune and inflammatory disease treatment applications in the prevention of the prevention of solid organ transplant rejection,antiviral[1], epilepsy[2],neuroprotective[3] and immunosuppress ive properties[4],Antitumor[5], anticonsultant[6-7], However, the importance of benzimidazoles[8] as p38MAP kinase inhibitors, B-Rafkinase, antimicrobial agents[9-11] anti-HIV[12]. Thiazoles are an important class of heterocyclic compounds found in many powerful biologically active molecules that also have pharmacological characteristics such as relative stability, starting material, built into a biocidal unit, and easy compound metabolism.

Benzothiazole ring system consists of thiazole fused with benzene which having multiple applications. Although they have been known from long ago to be biologically active, their varied biological features are still of great scientific interest. Refractometric[13-14] measurement results directly provided information on interactions between solvent and solvent. The current study was conducted in different percentage compositions. This study explores the potential of newly synthesized drugs, drug stability, as well as renovation and modification of traditional drugs used buy medical practitioners. This research work has been carried out taking all these things into consideration.

EXPERIMENTAL:

The 0.1 M solution of (1,2-Dihydro-benz[4,5] imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine (1e) and (1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine (2b) in different percentage of acetone-water and DMSO-water mixture were prepared. All weighing was made on contech electronic balance (±0.001g). The accuracy of density measurements was within 0.1 kg m^{-3}. The refractive indices of solvent mixture and solutions were measured by Abbes' refractometer was within (± 0.001). The densities of the solutions were determined by using density bottle. The temperature of prism box was maintained at 30+˚C. Initially, the refractometer was calibrated with glass piece (n = 1.5220) provided with the instrument.

OBSERVATION AND CALCULATION

The present work deals with the study of polarizability and molar refraction constant of (1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine and (1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine at 70%, 80% and 90 % Acetone-water and dioxane-water mixtures at different concentration temperatures at different composition. Intermolecular

interactions were calculated using the data obtained. As mentioned in the literature, the refractometric reading was taken.

The molar refraction of solvent Acetone-water and Dioxane-water mixtures were determined from,

$$R_{s\text{-}w} = X_1R_1 + X_2R_2$$

Where, R_1, R_2 are molar refractions of the solvents and water respectively.

The molar refraction represent actual or true volume of substance molecules in 1 mole. The molar refractions of solutions of compound in solvent–water mixture are determined from following equation

$$R_m = \frac{(n^2-1)}{(n^2+2)}\left\{\frac{[X_1M_1+X_2M+X_3M_3]}{d}\right\}$$

Where, n- refractive index of solution.

X_1 – mole fraction of solvent

X_2 – mole fraction of water

X_3 -mole fraction of solute

d – density of solution

M_1, M_2 & M_3 – molecular weights of solvent, water, solute respectively.

The molar refraction of compounds is calculated as,

$$R_{liq} = R_{mixture} - R_{s\text{-}w}$$

Polarizability constant (α) of compounds were calculated from the following relation-

$$R = \frac{4}{3}\pi N_o \alpha$$

N_o – Avogadro's number.

α – Polarizability constant

R- molar refraction

Table.1. Molar refraction of Acetone-water, Dioxane-water and DMSO-water mixture.

% of Solvent	R_m cm^3 $mole^{-1}$	
	Dioxane-water	Acetone-water
60	17.4208	14.7596
70	15.1808	13.1345
80	13.2694	11.6814
90	11.7993	10.6425
100	10.5996	9.7282

Table.2. Determination of Molar refraction and polarizability Constant at different concentrations for 70%, 80% and 90% of Acetone-water mixture.

Concentration (M)	Refractive Index n	R_{mix} (cm^3. $mole^{-1}$)	$\alpha x10^{-23}$ (cm^3)
70% Acetone-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.3645	15.5788	0.0618
0.05	1.3641	14.1522	0.0561
0.025	1.3632	13.0168	0.0516
0.0125	1.3623	11.8633	0.0471
0.00625	1.3599	10.8907	0.0432
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.3505	13.6488	0.0541
0.05	1.3496	12.2222	0.0485
0.025	1.3482	11.0868	0.0440

0.0125	1.3472	9.9333	0.0394
0.00625	1.3458	8.9607	0.0355
80% Acetone-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.3565	14.5788	0.0578
0.05	1.3554	13.1522	0.0522
0.025	1.3542	12.0168	0.0477
0.0125	1.3543	10.8633	0.0431
0.00625	1.3535	9.8907	0.0392
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.3535	13.6688	0.0542
0.05	1.3522	12.2422	0.0486
0.025	1.3405	11.1068	0.0441
0.0125	1.3493	9.9533	0.0395
0.00625	1.3479	8.9807	0.0356
90% Acetone-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.3571	14.8088	0.0587
0.05	1.3564	13.3822	0.0531
0.025	1.3554	12.2468	0.0486
0.0125	1.3549	11.0933	0.0440
0.00625	1.3534	10.1207	0.0401
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.3539	13.7088	0.0544
0.05	1.3526	12.2822	0.0487
0.025	1.3520	11.1468	0.0442
0.0125	1.3517	9.9933	0.0396
0.00625	1.3502	9.0207	0.0358

Table.3. Determination of Molar refraction and polarizability Constant at different concentrations for 70%, 80% and 90% of Dioxane-water mixture.

Concentration (M)	Refractive Index n	R_{mix} (cm^3. $mole^{-1}$)	$\alpha x10^{-23}$ (cm^3)
70% Dioxane-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.4245	17.71878	0.07028
0.05	1.4233	16.29222	0.06462
0.025	1.4223	15.15678	0.06012
0.0125	1.4208	14.00330	0.05554
0.00625	1.4197	13.03073	0.05168
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.4105	15.78878	0.06262
0.05	1.4102	14.36222	0.05697
0.025	1.4088	13.22678	0.05246
0.0125	1.4077	12.07330	0.04789
0.00625	1.4065	11.10073	0.04403
80% Dioxane-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.4165	16.71878	0.06631
0.05	1.4152	15.29222	0.06065
0.025	1.4148	14.15678	0.05615
0.0125	1.4133	13.00330	0.05158
0.00625	1.4121	12.03073	0.04772
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.4127	15.80878	0.06270
0.05	1.4122	14.38222	0.05704
0.025	1.4111	13.24678	0.05254

0.0125	1.4103	12.09330	0.04797
0.00625	1.4088	11.12073	0.04411
90% Dioxane-water			
(1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine			
0.1	1.4171	16.94878	0.06722
0.05	1.4168	15.52222	0.06157
0.025	1.4154	14.38678	0.05706
0.0125	1.4149	13.23330	0.05249
0.00625	1.4131	12.26073	0.04863
(1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine			
0.1	1.4139	15.84878	0.06286
0.05	1.4126	14.42222	0.05720
0.025	1.4118	13.28678	0.05270
0.0125	1.4112	12.13330	0.04812
0.00625	1.4099	11.16073	0.04427

RESULTS AND DISCUSSION:

The refractometric measurements are very important in medicinal, pharmaceutical and chemical sciences. It is very easy and low cost instrument. The values of molar refraction of Acetone-water and Dioxane-water mixture were presented in table 1. The molar refraction and polarizability constant of (1,2-Dihydro-benz[4,5]imidazo[2,1-c][1,2,4]triazin-3-ylidene)-(4-phenyl-thiazole-2-yl)-amine (1e) and (1-Benzothiazol-2yl-[1,2]diazetidin-3-ylidene)-(4-nitro-phenyl)-amine (2b) in 70%, 80% and 90% of Acetone-water and Dioxane-water mixtures were represented in table 2 and table 3 respectively. The molar refraction and polarizability constant increases with the increase in percentage composition of the binary liquid mixture. Refractive index increase with increase in concentration of 1e and 2b in binary solvent mixture. Due to the temporary dipole moment, this is related to the dispersion force and it is the molecular force which results from the temporary dipole moment. The cumulative interaction between dipole and dipole produces a weak force of dispersion that increases molar refraction and polarizability. This may be due to the weak effect of salvation that interprets weak interaction of the molecule. The weak solvent-solute interaction, which is good for drug and the drug receptor interactions, shows the best drug activity and drug effect and favours drug pharmacokinetics and pharmacodynamics.

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REFERENCES:-

1. Wolfe J F, Green Wood T D & Mulheron J M, Expert opinion on Therapeutic Patents, 8, 1998, 361.
2. Hangirgekar S.P et al. / Indo American Journal of Pharmaceutical Research . 2011:1(1); 153-157.
3. Wakode, A. W.; Burghate, A. S.; Wadhal,S. A. Indo American Journal of Pharmaceutical Research .**2014,** 4, 5010-5016.
4. Patnent C J, Kisner K, Stone R L & Delond D C, J Med Chem, 12, 1969, 1016.
5. (a) Bradshaw T D, Wrigley S, Shi D-F, Schultz R J, Paull K D & Steve MFG, Br J Cancer, 77, 1998,745; (b) Chua M-S, Shi D-F, Wrigley S, Bradshaw T D, Hutchinson I, Shaw P N, Barrett D A, Stanley L A & Stevens MFG, J Med chem, 42, 1999,381; (c) Leong C-O, Gasbell M, Martin E A, Heydon R, Bradshaw T. D & Steven MFG, Br J cancer, 88, 2003, 470.
6. Wakode, A. W.; Burghate, A. S.; Wadhal,S. A. Orient. J. Chem., Vol. **33**(3), 1207-1212 (2017)
7. Gunwaradana G P, Kohmoto S, Gunasekera S P, McConhell O J & Koehn F E, J Am Chem Soc, 110, 1988, 4856..
8. Wakode A.W.; Burghate, A. S.; Wadhal,S.A. Rasayan J. Chem.**2016**,4, 386-392.
9. Habib N S & EI-Hawash S A, Il Farmaco, 44, 1989, 1225.
10. Anton V D, Wai-Keung C, Anna V D & Lai-Wah C, J Fluorine Chem, 126, 2005, 759.
11. Omar M T, Egypt J Pharm Sci, 38, 1997, 281.
12. Ambadkar Dilip S. et. al. / Indo American Journal of Pharmaceutical Research . 2014:4(02);3505-3510.
13. Wakode A.W.; Burghate, A. S.; Wadhal S. A. IJRBAT, Special issue (2), Vol-V, July 2017.
14. Kshirsagar A. M., Tayade D. T., IJSRP, Volume 2, Issue 10, October 2012, 1-6.