



**STUDIES THE SOLVENT EFFECT ON MOLAR REFRACTION AND
POLARIZABILITY OF SUBSTITUTED HETEROCYCLIC DRUG IN DIFFERENT
SOLVENT AT 303K**

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ABSTRACT

Refractive index, molar refractivities and molar polarizability constant of Lisinopril have been studied in Ethanol, Methanol, Acetone, DMF, Dioxane and THF media at $30^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ temperature and in different concentrations (0.625×10^{-3} to $10.0 \times 10^{-3}\text{M}$). The values of molar refraction (R_m) and molar polarizability (α) constant are found to be decreased with decreasing concentration of solute in solvent.

KEYWORDS: Refractive index, molar refractivities and molar polarizability constant.

INTRODUCTION

Lisinopril (*N*2-[(1*S*)-1-carboxy-3-phenylpropyl]-L-lysyl-L-proline) is typically used for the treatment of hypertension, congestive heart failure, acute myocardial infarction, and diabetic nephropathy.^[1] Refractive index is one of the important properties of liquid. Measurement of refractive index shows very interesting applications in pharmaceutical, chemical, agriculture, food, oil and beverage industries. The refractive index is an important additive property of liquid. For pure hydrocarbon, one can get an idea of aromatic content of liquid using refractive index. Pharmacokinetics and pharmacodynamics parameters can also be determined by refractometric study. When a light beam passes from one substance to another, the beam is bending so that it travels in different direction. If it is passed from less dense to high denser medium it is refracted toward normal to form angle of refraction which is less than angle of incident. The refractive index is the ratio of angle of incident to the angle of refraction. It depends on the temperature and wave length of light. The extent of refraction depends on –i) The relative concentration of atom or molecule ii) The structure of atom or molecule.

So refractive index gives idea about geometry and structure of molecule. Refraction of light is additive property, but also depends on the structural arrangement of atom in molecule. Some time, this can be used to determine the structure of an unknown compound whose molecular formula is known.

Sangita Sharma^[2] has been studied density and refractive index of binary liquid mixture Eucalyptol with Hydrocarbon at different temperature. Oswal^[3] has been studied refractivity properties of some homologous series such as n-ethanoate, methyl alkanoates, ethyl alkanoates etc. were measured in the temperature range from 298.15 to 333.15⁰K. The properties of liquid such as refractive index, ultrasonic velocity and viscosity of binary mixture were studied by many workers.^[4-6] Yangang Liu^[7] has studied relationship of refractive index to mass density and consistency of the mixing rule use to calculate these two quantities of multicomponent mixture like ambient aerosols with the index-density relationship. Anand prakash^[8] has been studied Acoustical properties in binary mixture of cyclohexanone with different alcohols. Yadava^[9] has studied refractive indices of binary mixture of bromoalkane and non polar hydrocarbons, also studied molecular interaction between the components of binary mixtures. Sonune^[10] has been studied additive properties such as molar refractivity and molar polarizability constant of allopurinol, acenocoumarol, warfarin and amoxicillin in different media. The number of researcher were studied the relation between molar polarization, polarizability constant with concentration.^[11-13]

However, study of molar refractivity and molar polarizability constant of substituted heterocyclic drug such as lisinopril in non aqueous solvent such as ethanol, methanol, acetone, DMF, dioxane and THF under identical set of experimental condition. This could cover minifold aspect of solute-solvent interactions scanty. Therefore, the present work is undertaken to make the

systematic study of above substituted heterocyclic drug refractometrically at 25°C.

MATERIAL AND METHODS

Above substituted heterocyclic drug have most important life saving drug Lisinopril is typically used for the treatment of hypertension, congestive heart failure, acute myocardial infarction, and diabetic nephropathy. The solution of above compound is prepared in different solvent like ethanol, methanol, and acetone, DMF, Dioxane and THF by dissolving an appropriate amount by weight.

For density measurement all the weight of solution took on Contech balance (0.001gm). The refractive index of solutions is measured of different concentration (0.625x10⁻³ to 10x10⁻³) by Abbe's refractometer having accuracy with ±0.01 unit. The constant temperature of the prism box is maintained by circulating water from thermostat at 25°C. Refractometer was calibrated by using glass test piece of known refractive index supplied with the instrument.

The molar refraction of solvent and solution are determined by using Lorentz-Lorentz equation.

$$R_m = \frac{(n^2-1)}{(n^2+2)} \times \frac{M}{d} \quad (1)$$

$$R_m = \frac{(n^2-1)}{(n^2+2)} \times \frac{M}{d} = \frac{4}{3} \pi N \alpha \quad (2)$$

$$R_m = X_1 R_{m1} + X_2 R_{m2} \quad (3)$$

n- Refractive index M- Molecular weight

d- Density of solution

R_m- Molar refraction N- Avogadro's number

α- Molar polarizability constant X₁ and X₂ Mole fraction of solvent and solute in solution.

The molar refraction of solute can be calculated as

$$R_m(\text{Solute}) = R_m(\text{Solution}) - R_m(\text{Solvent})$$

The calculated value of molar refraction and molar polarizability constant shown in table 1 for different system.

RESULT AND DISCUSSION

The value of molar refraction (R_m) and molar polarizability constant (α) of polar solvents, like Ethanol, Methanol, and Acetone are found to be greater than non polar solvents like DMF, THF, and Dioxane. Because polar solvent contains H-bonding, may form complex with solute, but non polar solvent does not contains H-bonding and does not form complex with solute.

This may be characteristics to the fact that the dipole in the compound lies perpendicular to the longer axis of the molecule, which shows intermolecular attraction take place. This will be accompanied by increase the value of molar refraction and molar polarizability constant with increasing concentration of solution because of mutual compensation of dipoles.

From table (1), it could be seen that molar refractivity and molar polarizability constants decreases with decreasing in the concentration of solution.

Table-1: Molar polarization and polarizability constant (Lisinopril)

Conc ⁿ in Mole/lit.	Medium					
	Ethanol		Methanol		THF	
	R _m	α x 10 ⁻²⁶	R _m	α x 10 ⁻²⁶	R _m	α x 10 ⁻²⁶
10 x 10 ⁻³	0.1357	5.38	0.1330	2.27	0.1325	5.25
5 x 10 ⁻³	0.0681	2.70	0.0663	2.63	0.0663	2.63
2.5 x 10 ⁻³	0.0339	1.35	0.0332	1.31	0.0330	1.31
1.25 x 10 ⁻³	0.0168	0.666	0.0165	0.654	0.0163	0.644
0.625 x 10 ⁻³	0.0084	0.331	0.0082	0.323	0.0081	0.321
	DMF		Acetone		1,4 Dioxane	
	R _m	α x 10 ⁻²⁶	R _m	α x 10 ⁻²⁶	R _m	α x 10 ⁻²⁶
10 x 10 ⁻³	0.1048	4.15	0.1420	5.62	0.1235	4.89
5 x 10 ⁻³	.0522	2.07	0.0708	2.81	0.0615	2.44
2.5 x 10 ⁻³	0.0262	1.04	0.0355	1.40	0.0309	1.22
1.25 x 10 ⁻³	0.0126	0.515	0.0176	0.626	0.0159	0.606
0.625 x 10 ⁻³	0.0065	0.255	0.0087	0.346	0.0076	0.302

CONCLUSION

The drug-solvent molecular interactions with different structural modification in different solvents have been observed. The polarizability constant is increased with drug concentration in all solvents due to increase in

polarization of drug in solution. It shows strong solute – solvent interaction.

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