INTERNATIONAL JOURNAL OF PHARMACEUTICAL, CHEMICAL AND BIOLOGICAL SCIENCES

Available online at www.ijpcbs.com

Research Article

STUDIES ON FORMATION CONSTANT OF Co(II), Ni(II), Cr(III) AND Fe(III) ION COMPLEXES WITH SOME HETEROCYCLES BY p*H*-METRICALLY, SPECTROPHOTOMETRICALLY AND REFRACTOMETRICALLY

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ABSTRACT

Spectrophotometric investigation of Co(II), Ni(II) and Cr(III) and Fe(III) complexes with 3-(2-hydroxy-3-nitro-4-methylphenyl)5-phenylisoxazole (L_1) , 3-(2-hydroxyl-4-methyl phenyl)-5-phenyl isoxazoline (L_2), 1-phenyl-3-(2-hydroxy-3-bromo-4-methyl phenyl)-5-phenyl pyrazole (L_3), showed 1:1 and 1:2 complex formation between the p*H* range of 3.0 to 6.0 studied by Job's variation method at 0.1M ionic strength and 30°C ±1°C spectrophotometrically. The conditional stability constants are determined for 1:1 complexes at p*H* 3.0 and molar refraction and polarizibility constant for L_1, L_2 & L_3 at different percentage of dioxane have also been calculated.

Keywords: Isoxazole, Isoxazoline, Pyrazole, Spectrophotometry, Refractometry, p*H* metry.

INTRODUCTION

Heterocyclic rings have played an important role in medicinal chemistry, serving a key template central to the development of numerous important therapeutic agents. Amongst the many five membered heterocycles, considerable interest has been focused on the pyrazole, isoxazole and isoxazoline nuclei, which are known to possess a wide range of biological properties. Pyrazoles are known to participate in many enzymatic processes.[1] diarylpyrazoles have been identified as key pharmacophore in antimicrobial[2], analgesic[3] and anti-inflammatory agents[4]. Another interesting class of azoles containing one oxygen and one nitrogen atom at 1, 2- position are designated as isoxazoles and their partially reduced forms are referred as isoxazolines.

Isoxazole derivatives have also proved to be a versatile building block for the synthesis of several important synthetic units such as β-hydroxy ketones [5], □-amino alcohols[6], □□□-unsaturated oxime[7], and □-hydroxy nitriles[8]. Isoxazoles are known for its biological activities and pharmacological properties such as hypoglycaemic[9], antivascular/ anticancer[10], antimycobacterial[11] and anti-microbial activity[12]. Keeping in view analytical applications of these heterocyclic drugs, isoxazoles, isoxazolines, and pyrazoles, are selected as a ligand in the present study.

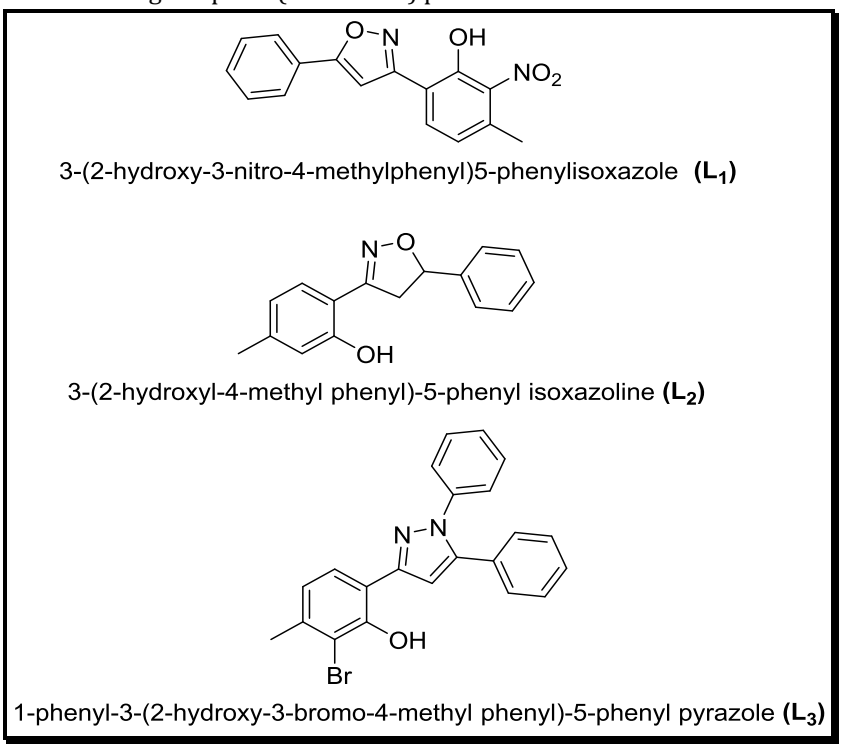
Determination of formation constant and stability constant of metal complexes with various ligands have been an important parameter for predicting the mode of drug action of these drugs. Many researchers made significant contribution to these kind of studies. Ali et al. studied the viscometric and refractive index behavior of glycine in

aqueous diol and found that paolarisability increases with increase in CH_2 group in diol.[13] Jani et al. studied stability complexes of Fe (II) and Fe (III) with 8-aceto-7-hydroxycoumarinhydrazone by Job's method by keeping metal:ligand ratio is 1:1.[14] Ramteke and Narwade studied the stability constants of chlorosubstituted pyrazoles with 3d series elements in 70 % dioxane-water mixture.[15] Shivraj et al. potentiometrically studied 3-amino-5-methylisoxazole schiff bases and their complexes with 3d series elements in solution [16]. Mukherjee et al. synthesized and studied monomeric copper (II) complex with a multidentate pyridylpyrazole ligand.[17] In addition to these other physical properties such as viscosity, refractive index and ultrasonic speed of binary mixtures are studied by many workers. Yadav et al. studied molecular interaction between some bromoalkane and non-polar hydrocarbon by refractometry.[18] Our research group has reported the formation constant of Al(III) Cr(III)and Fe(III) complexes with same substituted isoxazoles, isoxazolines and pyrazole.[19]

Herein, we report the study of conditional stability constants of transition metal ion complexes with heterocyclic drugs- isoxazoline, pyrazole and pyrazoline with Fe(III), Al(III) and Cr(III).

EXPERIMENTAL

Ligands L_1, L_2 and L_3 (Scheme 1) have been synthesized in laboratory by standard method. The nitrate salts of aluminium and iron and chromium and potassium nitrate (BDH) were used and their solutions (0.1M) were prepared in double distilled water. The solutions of potassium nitrate (0.1M) was prepared and used for maintaining ionic strength constant. Systronic spectrophotometer model No. 108 was used for measuring absorption of solution. The solution of ligands L_1, L_2, L_3 in different percentages of dioxane-water mixture were prepared. All weighing were made on Mechaniki Zaktady Precyzyjng Gdansk Balance, made in Poland (± 0.001 gm). The accuracy of density measurements was within 0.1% kgm^{-3}. The refractive indices of solvent mixture and solutions were measured by Abbe's refractometer. The accuracy of Abbe's refractometer was within ± 0.001 unit. The temperature of the prism box was maintained constant by circulating water from thermostat maintained at 30 (±0.1°C). Initially, the refractometer was calibrated with glass piece (n = 1.5220) provided with the instrument.



Scheme1: Structures of the ligands (L_1, L_2 and L_3) used in the study

The molar refraction of solvent, dioxane-water mixtures are determined as -

$$R_{D-W} = X_1R_1 + X_2R_2$$

where, R_1 and R_2 are molar refraction of dioxane and water respectively.

The molar refraction represents actual or true volume of the substance molecules in 1 mole. The molar refraction of solutions of ligand in dioxane-water mixture is determined as-

$$R_{Mixture} = [(n^2 - 1)/(n^2 + 2)] \{[X_1M_1 + X_2M_2 + X_3M_3]/d\}$$

where, n is the refractive index of solution, X_1 is mole fraction of dioxane, X_2 is mole fraction of water, X_3 is mole fraction of solute, M_1, M_2 and M_3 are molecular weights of dioxane, water and solute respectively. 'd' is the density of solution.

The molar refraction of ligand was calculated as –

$$R_{Lig.} = R_{Mixture} - R_{D-W}$$

RESULTS AND DISCUSSION

pH-Metric

pH-Metric work has been done with a limited aim to compare the formation constant value obtained spectrophotometrically. The agreement between the formation constant values from above technique is found to be satisfactory (Table 1). The difference between log K_1 and log K_2 is smaller in some of the systems. It seems, therefore, that both the 1:1 and 1:2 complexes are formed simultaneously and not in a stepwise process.

For each system the pH values at which metal complex formation started and hydrolysis commenced have been tabulated and data are presented in Table 2.

Spectrophotometric Measurement by Job's Method

Jobs variation method has been used to know the nature of complexes. The compositions of metal ion solution (1 x 10^{-2} M) and ligand (20 x 10^{-2} M) were prepared in series. Ionic strength was maintained constant (0.1 M) by adding an appropriate amount of 0.1 M KNO_3 solution in 10 ml volume. λ_{max} was determined using one of the composition at which there is maximum absorption.

The absorption for all the compositions was recorded at a constant wavelength (λ_{max}). The data of absorption and percentage composition of metal ion and ligand solution at constant *p*H can be used and curves were constructed.

It was observed that 1:1 complex formation curve occur in pH range of 3 to 4 and 1:2 complex formation in the pH range of 4 & 5. Each solution is diluted up to 15 ml and recorded absorptions at same (λ_{max}). Conditional stability constants of metal-ligand complexes were calculated for all the systems using following equation.

$$K = \frac{X}{(a_1-x)(b_1-x)} = \frac{X}{(a_2-x)(b_2-x)}$$

K = Conditional stability const. of complex
x = Concentration of complex
a_1 & a_2 = Concentration of metal ions
b_1 & b_2 = Concentration of ligand

Conditional stability constant of metal-ligand complexes were calculated and presented in table 3.

The conditional stability constants are found to be slightly smaller than real stability constants, this is because of the concentration of free acid at particular pH was not taken into account and may be due to variation in temperature.

Al (III), Cr(III) and Fe(III) act as hard acids and forms 1:1 complexes in the pH range 2.5 to 3.5. Stability constant depends upon the size of cations. It could be seen from table-1 that reduction in the value of stability constant of Al(III) complexes is due to its smaller cationic size as compared to cationic size of Cr(III) and Fe(III). The order of stability constant is presented as Al(III) < Cr(III) < Fe(III).

Refractometric measurement

The polarizibility constant (α) of ligand is calculated from the following relation,

$$R_{Lig.} = (4/3)\,\pi\, N_0\, \alpha$$

where, N_0 is Avogadro's number.

The value of molar refraction and polarizibility constants of ligand L_1, L_2 and L_3 in different percentage of dioxane-water mixture are represented in Table 4.

It shows that with increase in percentage of dioxane, the molar polarizibility constant of ligand increases but there is no regular order of molar refractivity with increase in percentage of dioxane-water mixture. This may be due to the fact of effect of bulky solvent dioxane. This may be also attributed to the fact that the dipole in the ligand lies perpendicular to the longer axis of the molecules and with increase in the percentage of dioxane causing decrease in dielectric constant of medium, considerable dipole association (inter molecular attraction) takes place which would be accompanied by increase in polarizibility constant because of mutual compensation of the dipoles.

CONCLUSION

It could be seen from Table (1), that there is no an appreciable difference between log K_1 and log K_2 values. This indicates the formation of 1:1 and 1:2 complexes simultaneously. It means antibiotic ligands used are found to be weak complexing agents. The change in the colour with respect to p*H* value of solution and deviation of ligand curve from metal ion curve also show the commencement of complex formation

The value of molar refraction and polarizibility constants of ligand L_1, L_2 and L_3 in different percentage of dioxane-water mixture are represented in Table 4. It shows that with increase in percentage of dioxane, the molar polarizibility constant of ligand increases but there is no regular order of molar refractivity with increase in percentage of dioxane-water mixture. This may be due to the fact of effect of bulky solvent dioxane.

ACKNOWLEDGEMENT

The authors are thankful to the Director and Head of Chemistry Department, Govt. Vidarbha Institute of Science & Humanities, Amravati.

Table 1: Metal-Ligand Stability Constants by Different Methods

System	Constants	Method	
		Half Integral	Pointwise
Fe(III) - (L_1)	log K_1	3.2966	4.1658
	log K_2	3.1172	3.2126
Cr(II) - (L_1)	log K_1	5.0791	5.066
	log K_2	3.5196	5.0761
Ni(II) - (L_1)	log K_1	4.696	6.0779
	log K_2	3.119	3.2254
Co(II) - (L_1)	log K_1	5.195	5.086
	log K_2	3.619	3.545
Co(II) - (L2)	log K_1	6.396	6.2127
	log K_2	4.719	4.1626
Ni(II) - (L3)	log K_1	3.591	6.4901
	log K_2	2.217	4.3284

Table 2: pH values at which metal complex formation started and hydrolysis commenced

Metal Ion	pH at the commencement of the Hydrolysis	pH at the commencement of complete formation
Co(II)	5.9	4.70
Ni(II)	6.0	5.20
Cr(III)	5.5	5.10
Fe(III)	6.5	5.90

Table 3: Determination of conditional stability of metal-ligand complex by Job's method

System	Concentration of complex (x) mole lit^{-1}	Conditional stability constant (K)	Log K
1) Al(III) - L_2	2.8939 x 10^{-3}	1.2256 x 10^{-3}	0.0883
2) Fe(III) - L_1	2.9775 x 10^{-3}	2.514780 x 10^{-3}	0.4004
3) Cr(III) - L_3	2.91666 x 10^{-3}	1.263528 x 10^{-3}	0.10158
4) Cr(III) - L_1	2.91509 x 10^{-3}	1.462208 x 10^{-3}	0.16500

Table 4: Molar refraction and polarizibility constant for L1, L2 and L3 at different percentage of dioxane

% of Dioxane	Ligand –(L_1)		Ligand –(L_2)		Ligand –(L_3)	
	[R] cm^3 $mole^{-1}$	α x 10^{-23} $mole^{-1}$	[R] cm^3 $mole^{-1}$	α x 10^{-23} $mole^{-1}$	[R] cm^3 $mole^{-1}$	α x 10^{-23} $mole^{-1}$
65%	2.957062	0.1172680	2.514762	0.0997277	2.5224062	0.1072680
70%	2.504169	0.0993076	2.504169	0.0993076	2.5192615	0.0189307
75%	2.498867	0.0990974	2.957062	0.1172680	2.9467824	0.1879091
80%	2.509468	0.0995178	2.514762	0.0997277	2.5386743	0.0995178
85%	2.498867	0.0990974	2.514762	0.0997277	2.5376238	0.1279746
90%	2.450978	0.0971982	2.640711	0.1047225	2.6547189	0.0977192
92.5%	2.461646	0.0976220	2.450978	0.0971982	2.4785720	0.1976220

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