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PHYSICO-CHEMICAL AND SPECTROPHOTOMETRIC STUDY OF STABILITY CONSTANT OF CU(II) METAL COMPLEXES WITH LIGANDS 2-(4-(HYDROXYMETHYL)-1-PHENYL-1H-PYRAZOL-3-YL) PHENOLS DERIVATIVES AT DIFFERENT TEMPERATURE

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ABSTRACT
Complexes of copper (II) with 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl)phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) ligands derived from reaction of 3-aryl-1-phenyl-1H-pyrazole-4- carbaldehyde with $NaBH_4$ have been prepared. All the complexes have been characterized by elemental analyses, conductance measurement, magnetic moment, infrared, NMR, ESR and electronic spectral studies. The complexes were found to have stoichiometry (1:2), ML_2. On the basis of spectral and magnetic studies square planar geometry has been assigned for these complexes. The formation of copper(II) complex with (H_2L^1) and (H_2L^2) has been studied spectrophotometrically at an absorption maximum of 658 nm at different temperatures. The data shows that copper(II) and (H_2L^1) and (H_2L^2) combine in the molar ratio of 1: 2 at pH 5.0. The stability constants of the complexes were calculated to be 14×10^4, 9.33×10^4 and 4.39×10^4 and $3.18x10^4$, $3.36x10^4$, $5.98x10^4$ for (H_2L^1) and (H_2L^2) respectively by continuous variation method and 0.45×10^4, 0.58×10^4, and 0.51×10^4 and 0.62×10^4, 0.51×10^4, 0.48×10^4 for (H_2L^1) and (H_2L^2) respectively by mole ratio method at 30, 35 and 40°C, respectively.

KEYWORDS
Pyrazole, Magnetic moment, Spectrophotometry and Stability constant.

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INTRODUCTON
Bucher[1] was described for the first time about the pyrazole, who obtained it by decarboxylation of pyrazole-3, 4, 5-tricarboxylic acid in 1889. Wide range of biological activity have been reported for pyrazole derivatives. In the field of drug discovery, pyrazoles have been tremendously used and therefore pyrazole ring constitutes a relevant

synthetic target in pharmaceutical industry. Celecoxib is the commercial available pyrazole derivative is use in the treatment of acute pain, painful menstruation and menstrual symptoms, and to reduce numbers of colon and rectum polyps in patients with familial adenomatous polyposis[2,3]. Tepoxalin is also a commercial available pyrazole derivative is use non-steroidal anti-inflammatory drug approved for veterinary use in the United States and the European Union[4-6]. There are a number of book chapters[7,8] and literature reviews[9-11] dedicated to the synthesis of pyrazoles and condensed pyrazoles. Pyrazole synthesis involves the cyclocondensation of hydrazine, or hydrazine derivatives, with 1, 3-dicarbonyl compounds is the first general method. While a symmetrical 1, 3-dicarbonyl gives a single pyrazole isomer, unsymmetrical-substituted dicarbonyl can give one or both isomers[12]. On the basis of literature survey, in the present work, we report the synthesis, characterization and spectrophotometric study of stability constant of Cu(II) metal complexes with ligands 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) at different temperature.

MATERIAL AND METHODS

All the chemicals and solvents used were of AR grade were obtained from Sisco-chem. Industries. The metal salts were purchased from commercial sources. Metal contents were estimated using standard methods[13]. The electronic spectral studies of the complexes were carried out by using an Elico SL 159 spectrophotometer in the 200-1000nm ranges in DMF solution (10^{-3}). The elemental analyses data of the ligands and complexes were obtained HERAEUS C, H, N-O rapid analyzer. E.S.R measurements were carried out on a VARAN E-109 GHz., by taking DPPH as the reference with the field set at 3200 Gauss. The magnetic susceptibilities were determined by the Faraday method using a Model 300 Lewis Coil Force Magnetometer of one Tesla field strength at room temperature, the instrument being calibrated with Hg [Co (SCN)$_4$][14,15].

All melting points were uncorrected and measured using an Electro-thermal IA 9100 apparatus (Shimadzu, Japan). Infra-Red spectral study of the prepared ligands and complexes were recorded by using Perkin-Elmer 1650 spectrophotometer (Shimadzu). As potassium bromide pellets. Proton NMR (^{1}H NMR) spectra were recorded on a Varian Gemini 180 spectrometer (Varian, UK) and chemical shifts were expressed as (ppm) values against TMS as internal reference.

Electric spectral measurements were performed on a UV- 1700 Shimadzu double beam spectrophotometer (Japan) using matched 10 mm quartz cells. Elico pH meter, was used for pH measurements and calibrated with standard buffer solutions. Copper (II) sulphate pentahydrate and other chemicals used were of AR grade was purchased from Merck, Germany. Double-distilled water was used throughout this study.

General procedure for the preparation of ligands 3-aryl-1-phenyl-1H-pyrazole-4-carbaldehyde

The derivatives of 2-hydroxyacetophenone phenylhydrazone (0.01 mol) was dissolved in DMF (15 ml) and then POCl$_3$ (0.03 mol) was added drop wise at 0° C, the reaction mixture warmed at room temperature and heated at 60-70° C for 2.5-3h. The reaction mixture was poured into crushed ice and then neutralized with 10% aqueous NaOH solution. The precipitate was filtered, strongly washed with water and crystallized from ethanol, yielding 84-88%.

2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols

To a solution of 3-aryl-1-phenyl-1H-pyrazole-4-carbaldehyde (1.2 m mol) in methanol (30 ml), NaBH4 (3.6 m mol) was added at 0°C slowly. Then the mixture of reaction was removed to room temperature for 2 h. Then the reaction mixture was poured onto crushed ice and neutralized by hydrochloric acid. 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) was precipitated and filtered. The crud compounds were crystallized from ethanol.

Preparation of metal complexes

The preparation of the complexes were performed by adding a hot solution of each of (0.16 g, 0.951m mole) copper chloride $CuCl_2.2H_2O$, (0.23g, 0.951m mole) in absolute ethanol (5 ml) to (0.20g, 0.951m mole) of H_2L^1 and H_2L^2 in absolute ethanol (10 ml). The mixtures were refluxed with stirring for six hours, the resulting precipitates were filtered and washed with diethyl ether and recrystallized from hot ethanol, and it was then dried at room temperature. Table No.1 shows the physical properties of the ligands and metal complexes.

RESULTS AND DISCUSSION

The prepared pyrazoline ligands and their complexes were characterized based on elemental analyses, conductance measurement, magnetic moment, infrared, NMR, ESR and electronic spectral studies. All the complexes were found to have stoichiometry (1:2) ML on the basis of elemental analysis. The magnetic moment μ_{eff} of the ligand complexes was measured by Faraday method[16] at room temperature. The μ_{eff} values for the complexes $Cu(H_2L^1)$ and $Cu(H_2L^2)$ were 1.65 and 1.63 BM respectively, indicating these complexes are square planar geometry. The molar conductivities of the complexes were measured using Johns and Brad Method[17] at room temperature $(1x10^{-3}$ M) in DMF. The molar conductance values of the complexes were high indicating that they are electrolytic in nature. IR spectra of ligand show a broad medium intensity band in the region 3450-$3300cm^{-1}$ due to phenolic-OH[18], in complexes these bands were not observed due to the coordination through O via deprotonation of phenolic-OH. The band in the region 1640-$1590cm^{-1}$ is assigned to C=N group in the complexes, indicating that the involvement in coordination of metal ions through nitrogen. In complexes the bands due to C=N group are shifted to lower frequency by 30-$20cm^{-1}$. In complexes IR spectra of ligand show a broad medium intensity band in the region 3450-$3300cm^{-1}$ due to phenolic-OH[19], in complexes these bands were lightly observed due to the coordination through O via deprotonation of phenolic-OH and one phenolic-OH remains as it is.

The electronic spectral study for the ligands and their complexes were carried out, the ligands H_2L^1 and H_2L^2 showed aromatic band around 223nm attributed to benzene ring $\pi–\pi^*$ transition, while the band around 343 nm are ascribed to the $n–\pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base[20]. For CuL^1, and CuL^2 complex showed a broad band with maximum at 412 nm due to metal to ligand charge transfer[21]. The band maxima observed in the present study for CuL^2 complex is at $16120cm^{-1}$. These observation suggest that the Copper(II) complexes with ligands 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) ligands are having Square planar geometries.

The Schiff bases and corresponding complexes were scanned for ^1H NMR spectra in DMSO-d_6 solvent in the range of 0-15 δ(ppm) down field of TMS. The ^1H NMR spectrum of these ligands 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) in DMSO – solvent gave well-resolved multiplets at 7.55δ–7.84δ corresponding to aromatic protons. In the complexes these signals were shifted to lower field were observed at 7.30-7.77 δ due to complexation. In ligands and complexes the multiplets observed in the range 7.23-7.45 δ(ppm) due to resolution of aromatic protons. The resolution of azomethine protons at 8.22-8.45 δ(ppm) in ligands but in complexes these signals are shifted to down field. The signals at 12.15 δ(ppm) due to –OH (phenolic) group of ligands are disappeared in complexes due to -OH (phenolic) group is involved in bonding through oxygen with metal ions.

The X-band ESR spectrum of the polycrystalline copper(II) complexes has been recorded at room temperature, measurements on homogeneous powder sample give $g_{\parallel}$ and $g_{\perp}$ values only as observed in the case of copper complexes under study. The width and shapes of the absorption lines

offer a means of studying the magnetic coupling and extraction within substance[22]. The $g\|$ and $g\perp$ values are calculated according to the procedure indicated by Peisach and Blumberg[35]. In the present investigation, the observed $g\|$ value is 2.02, indicate that the complex is covalent in nature $g\| >$ $g\perp$. 2.0036), g_{av} it is evident that the unpaired electron lies predominantly in the $dx^2 -y^2$ orbital of Cu (II) ion, the g values are related by the expression[22]. Kivelsen and Nieman[23-25]. Have shown that the $g\|$ is moderately sensitive function of metal ligand covalently. For ionic environment $g\|$ is normally 2.4 or larger and for more covalent environment it is less than 2.3. G = {$(g\|-2)/ (g\perp-2)$} which measures the measures the exchange interaction between copper centre in the polycrystalline solid. In the present study, all copper (II) complexes have G values in the range of 2.16 – 2.19 indicating the exchange interaction of the copper centers. According to Hathaway[26] if value of G is greater than four, the exchange interaction is negligible, where as he value of G is less than four, considerable exchange interaction is indicated in the solid complex. Based on the above observations of elemental analysis, IR, electronic spectral data, ^{1}H NMR spectra, magnetic measurements, conductance measurements, proposed the square planar structure for CuL[1] and CuL[2]complexes.

The reaction of Ligands H_2L^1 and H_2L^2 with copper(II) sulfate pentahydrate was investigated at pH 5.0 + 0.05 buffer solutions, at three temperatures, *i.e.* 25, 35, and 45 °C. The absorption spectra of the pyrazoline derivatives as ligands with copper(II) sulphate pentahydrate formed a dark blue, water soluble complexes. The complexes gave an absorption peak at 638 nm (Figure No.2) and was used for the analytical measurements. Under the same conditions, pure ligands H_2L^1 and H_2L^2 does not absorb significantly over the investigated wavelength range. Water behaves as a weak field ligand so copper-aquo complex acts as a labile complex, which can be easily replaced by ligands H_2L^1 and H_2L^2 to form a stable complexes ML_2 (λmax = 638 nm). Concentration effects of copper(II) sulphate pentahydrate on the formation of Cu with ligands H_2L^1 and H_2L^2 complexes showed that a two-fold mole ratio of reagent to analyze is necessary for maximum complex formation. The color development was observed immediately and the absorbance remained unchanged. Metal ion binding is not able to change some conformational features of ligands.

The Composition of Complex and Stability Constant
The stochiometric ratio of H_2L^1 and H_2L^2 to Cu(II) in the complex was determined by Job's method of equimolar solutions[27,28]. Copper(II) sulfate pentahydrate standard solution 3×10^{-2} M was pippetted into seven volumetric flasks (0, 1, 2, 3, - - -6 mL) and an aliquot of 3×10^{-2} M H_2L^1 and H_2L^2 (6, 5, 4, -- - 0ml) was added, respectively, keeping the mole ratio constant. For all the prepared complexes absorbance measurements were made at 638 nm at three temperatures, *i.e.* 30, 35, and 40°C (Table No.1).
The curve displayed a maximum at a mole fraction χ_{metal} = 1, which indicates the formation of complex with 1:2 metal to ligand ratio. The corresponding equation used in this study for Job's method is as follows: $K_f = \frac{[ML]}{[m][L]}$, $K_f = \frac{A_2/A_1}{C_M(1-A_2/A_1)^2}$

Where, A_1 = absorbance at break point, A_2 = actual absorbance, C_M = concentration of metal, and C_L = concentration of ligand. The absorbance have been measured for the mole ratio method[29-30] at constant Cu(II) concentration (06×10^{-4}M) and varying ligands H_2L^1 and H_2L^2 concentrations (0 to 14×10^{-4}M) at 638 nm at different temperatures (Table No.3 and No.4), a sharp band was observed at 1:2 mole ratio for all Cu(II) complexes (Figure No.4).
The following equation is used for mole ratio method:
$$K_f = \frac{A/\varepsilon b}{(C_M - A/\varepsilon b)(C_L - A/\varepsilon b)}$$
Where ε_b = molar absorptivity constant, and A = absorbance at peak point.
On the basis of data obtained by using Job's and Mole ratio methods, the stability constants have been determined and the mean value of K_f obtained by two different methods are in fair agreement (Table No.5).

Table No.1: Analytical data of the ligands and their complexes

S.No	Ligands/ Complexes	Yield (%)	M.p (°C)	Molecular Formula	Elemental analysis found/(calcd)				
					M	C	H	N	Cl
1	H_2L^1 Ligand-1	86	146-147	$C_{16}H_{11}O_2N_2Cl$	-	64.45 (64.33)	3.75 (3.71)	9.42 (9.37)	11.93 (11.86)
2	H_2L^2 Ligand-2	89	146-147	$C_{16}H_{10}O_2N_2Cl_2$	-	57.75 (57.68)	3.09 (3.02)	8.45 (8.40)	11.36 (11.28)
3	Cu(L^1)	57	225-227	$Cu(C_{16}H_{10}O_2N_2Cl)_2$	9.61	58.19 (58.14)	3.42 (3.35)	8.55 (8.47)	10.65 (10.72)
4	Cu(L^2)	56	237-239	$Cu(C_{16}H_9O_2N_2Cl_2)_2$	8.70	52.55 (52.65)	2.66 (2.76)	7.65 (7.67)	19.33 (19.43)

The values given in the parenthesis are calculated one.

Table No.2: Jobs continues variation method, experimental data of copper(II) complexes with 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) at different temperature

S.No	Metal Conc. (×10⁻⁴ moles)	Ligand Conc. (×10⁻⁴ moles)	χ_{Cu}	Absorbance at 638 nm		
				30°C	35°C	40°C
1	0	30	0.0	0.035	0.045	0.030
2	5	25	0.142	0.152	0.155	0.152
3	10	20	0.29	0.257	0.264	0.277
4	15	15	0.43	0.358	0.345	0.356
5	20	10	0.57	0.275	0.287	0.285
6	25	5	0.71	0.177	0.172	0.171
7	30	0	1	0.059	0.062	0.067

Table No.3: Experimental data of copper(II) complexes with 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) at different temperature Jobs continues variation method

S.No	Metal Conc. (×10⁻⁴ moles)	Ligand Conc. (×10⁻⁴ moles)	χ_{Cu}	Absorbance at 638 nm		
				30°C	35°C	40°C
1	0	30	0.0	0.032	0.045	0.030
2	5	25	0.142	0.155	0.155	0.146
3	10	20	0.29	0.265	0.266	0.277
4	15	15	0.43	0.331	0.355	0.356
5	20	10	0.57	0.275	0.285	0.284
6	25	5	0.71	0.189	0.166	0.167
7	30	0	1	0.063	0.067	0.066

Table No.4: Mole ratio method, experimental data of copper(II) complexes with4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1)

S.No	Metal conc. (10^{-4} mole)	Ligand conc. (10^{-4} mole)	Absorbance at 638 nm		
			30°C	35°C	40°C
1	06	0	0.0	0.0	0.0
2	06	2	0.082	0.089	0.075
3	06	4	0.140	0.144	0.135
4	06	6	0.163	0.166	0.167
5	06	8	0.174	0.186	0.170
6	06	10	0.184	0.190	0.175
7	06	12	0.186	0.193	0.184
8	06	14	0.195	0.198	0.196

Table No.5: Mole ratio method, experimental data of copper(II) complexes 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2)

S.No	Metal conc. (10^{-4} mole)	Ligand conc. (10^{-4} mole)	Absorbance at 638 nm		
			30°C	35°C	40°C
1	06	0	0.0	0.0	0.0
2	06	2	0.068	0.073	0.064
3	06	4	0.142	0.146	0.144
4	06	6	0.161	0.159	0.165
5	06	8	0.175	0.177	0.175
6	06	10	0.183	0.187	0.184
7	06	12	0.187	0.190	0.188

Table No.6: Metal-ligand formation constants calculated from continuous variation method and mole ratio method at 30^0C, 35^0C and 40^0C and P^H of 5.0 ± 0.05

S.No	Methods	Metal: Ligand	Formation Constants at temperatures		
			30^0C	35^0C	40^0C
1	Continuous variation method Copper(II) complexes with (H_2L^1)	1:2	14×10^4	9.33×10^4	4.39×10^4
2	Copper(II) complexes with (H_2L^2)	1:2	3.18×10^4	3.36×10^4	5.98×10^4
3	Mole ratio method Copper(II) complexes with (H_2L^1)	1:2	0.45×10^4	0.58×10^4	0.51×10^4
4	Copper(II) complexes with (H_2L^1)	1:2	0.62×10^4	0.51×10^4	0.48×10^4
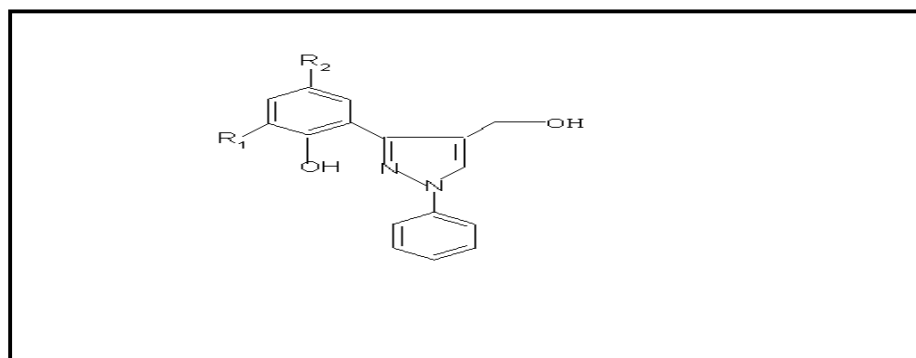
Figure No.1: Pyrazoline derivatives as ligands H_2L^1 R_1= H, R_2=Cl and H_2L^2 R_2=Cl, R_2=Cl
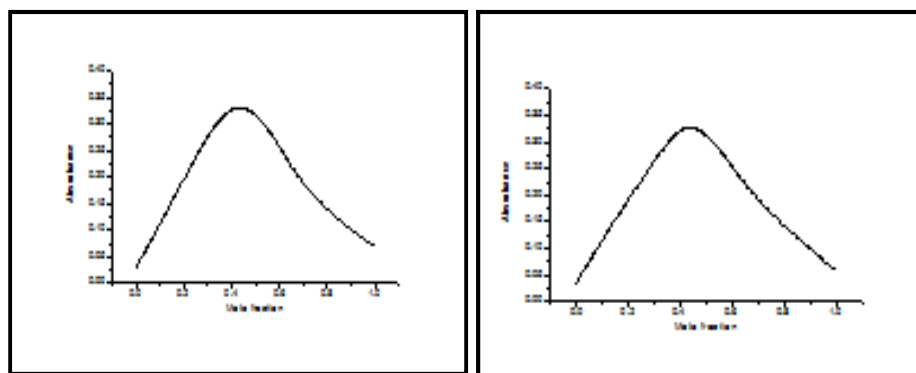
Cu(II) complex with H_2L^2 at 35ºC   Cu(II) complex with H_2L^2 at 40ºC

Figure No.2: Representative Jobs curves of equimolar solutions of Copper(II) complexes with (H_2L^1) and (H_2L^2) at 35^0C and 40^0C
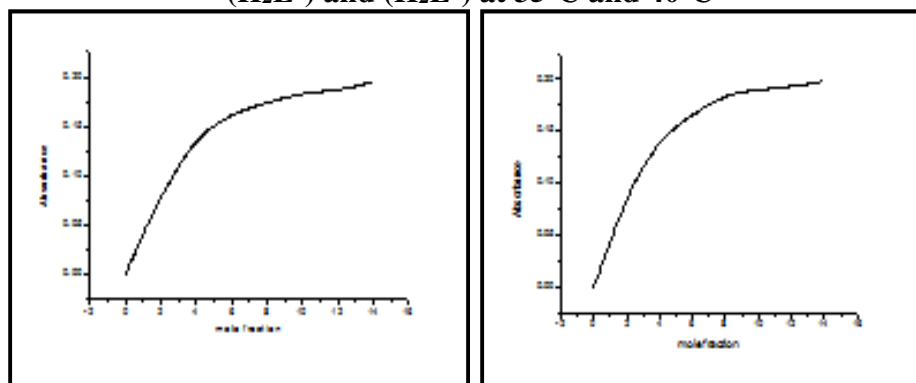
Cu(II) complex with H_2L^1 at 30^0C   Cu(II) complex with H_2L^1 at 35^0C

Figure No.3: Representative Mole ratio curves for Copper(II) complexes with (H_2L^1) 35^0C and 40^0C

CONCLUSION

In this paper reported that the preparation and characterization of a new bidentate ligands namely: 4-chloro-2-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenols (H_2L^1) and 2, 4-dichloro-6-(4-(hydroxymethyl)-1-phenyl-1H-pyrazol-3-yl) phenol (H_2L^2) and their complexes. All the complexes are colored, stable in air and insoluble in water and common solvents but soluble in polar solvent like DMF and DMSO. The analytical data obtained were suggested that 1:2(M: L) stoichiometry for all complexes. The prepared complexes have electrolytic nature. Based on the above observations of IR, electronic spectral data, ^{1}H NMR spectra, magnetic, conductance measurements, proposed the square planar structure for CuL^1 and CuL^2complexes. The Copper(II) complexes with (H_2L^1) and $(H_2L^2$ benefits from a moderately high formation constant in acidic media.

The proposed method provides an appropriate selectivity and sensitivity for easy determination of Cu(II) ions. One of the advantages of this method is directly measuring of Cu(II) in various aqueous media, such as pharmaceutical samples. Pyrazoline derivative H_2L^1 and H_2L^2, forms a reasonably stable complexes with Cu^{2+} ions. The stability constant data obtained from Job's method corresponds well with the analogous values obtained by the mole ratio method. Formation of complexes takes place in acidic medium at room temperature. Owing to high formation constant at body temperature, pyrazoline derivative H_2L^1 and H_2L^2 intake can remove copper (an essential trace element) from the body. A new type of complex as a Copper(II) complexes with (H_2L^1) and (H_2L^2) was developed for determination of Cu(II) with spectrophotometric method.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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