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Spectrophotometric Determination of Chemical Speciation of Complexes of L-Dopa with Co(II), Ni(II) and Cu(II).

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ABSTRACT

Chemical speciation of complexes of Co(II), Ni(II) and Cu(II) with L-Dopa (dopa) has been studied spectrophotometrically. The complexations were carried out at different pH ranges at the wavelengths of respective complexes. The stoichiometries of the complexes were determined using Job's continuous variation method and the value was found to be 1:2 metals to ligand ratio. Stability constant values were calculated using the continuous variation method. The complexes were found to be stable over the pH range used as there was slight change in the color intensity and absorbance values.

Keywords: Cobalt(II), Nickel(II), Copper(II), Spectrophotometry, Stability constants, Toxicity.

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INTRODUCTION

Metal ions, especially transition metal ions, possess the ability to form complexes with ions, organic and inorganic molecules or ions called ligands. Stability constants of metal ion complexes of various ligands and especially chelating ligands using different methods such as potentiometric and spectrophotometric techniques have been determined [1-5]. Stability constant of a complex ion is influenced by factors such as ligand type, metal ion type, counter-ions and solvent [6].

Although owing to versatile properties of Schiff's bases they have multifarious roles in diverse fields, viz. industries [7], analytical [8,9], coordination [10-12] and organic chemistry [13,14], agriculture [15], medical sciences [16-18] etc. but ketoazomethines exhibiting novel ligation properties in forming heteropolynuclear [19] and isomeric complexes [20] and also adducts in unusual coordination numbers [21,22] with transition metals attract high attention as ligands.

Chelating ligands are useful in detoxification of poisonous metals and can form more bonds to the metal ion thereby enhancing higher affinity for the metal ions when compared to the monodentate ligands.

Cobalt(II), nickel(II) and copper(II) are associated with several enzymes [23,24] and any variation in their concentration leads to metabolic disorders [25]. Hence speciation study of essential metal ion complexes is useful to understand the role played by the active site cavities in biological molecules and the bonding behavior of protein residues with the metal ions. In biological fluids, metal ions exist in non-exchangeable form as in metallo-proteins or loosely bound to some bioligands as in metal-activated proteins. The loosely bound metal ions are in equilibrium with simple metal ions present in the bio-fluids. These simultaneous equilibria involving a variety of metal ions and ligands are important in bio-fluids [26].

The formation of metal complexes of dopa was reviewed by Gergely [27] and Pettit [28]. Dopa is a naturally occurring dietary supplement and psychoactive drug found in certain kinds of food and herbs. Besides its natural and essential biological role dopa is a popular drug in the treatment of manganese poisoning and Parkinson's disease [29,30] which are accompanied by neurologically similar sequels [31]. Dopa is also a popular drug in the treatment of dopamine-responsive dystonia and to increase dopamine concentration, since it is capable of crossing the blood brain barrier, where dopamine itself cannot. Once dopa enters the central nervous system (CNS) it is converted into dopamine by the enzyme aromatic L-amino acid decarboxylase, also known as dopadecarboxylase. However, conversion to dopamine also occurs in the peripheral tissues, causing adverse effects and decreasing the availability of dopamine to the CNS; it is the standard practice to co-administer a peripheral dopa decarboxylase inhibitor.

Cobalt is an essential element for life in minute amounts (10 mg/day), at higher levels of exposure it shows mutagenic and carcinogenic effects [32]. Minot and Murphy [33] discovered that pernicious anemia can be treated by feeding the patient with large amounts of liver which contains vitamin B₁₂. Trace amounts of vitamin B₁₂ are essential for the synthesis of hemoglobin. Its deficiency causes anemia. Besides cobalt is involved in the production of red blood cells and is important for the proper functioning of the nervous system as it can help in creating a myelin sheath.

Nickel plays numerous roles in the biology of microorganisms and plants [34-36]. Urease, an enzyme which assists in the hydrolysis of urea, contains nickel. Other nickel-containing enzymes include a class of superoxide dismutase [37] and a glyoxalase [38]. Copper is essential in all plants and animals. The human body contains copper at a level of about 1.4 to 2.1 mg/kg weight of human body [39].

Although the above said metals are biologically essential, they become toxic beyond certain concentrations. Biological system has homeostasis to keep the concentration of these metals. For example, copper exhibits acute copper toxicosis. Acute copper toxicosis, manifested by hemolysis, headache, febrile reactions, prostration, and GI symptoms, was observed in one child after a solution containing copper sulfate was applied to burned skin during a debridement procedure and in numerous patients after inadvertent introduction of copper into the circulating blood during hemodialysis. Following acute ingestion of copper salts in amounts that exceed approximately 1 g, systemic effects are generally observed. The effects include GI mucosal ulcerations and bleeding, acute hemolysis and hemoglobinuria, hepatic necrosis with jaundice, nephropathy with azotemia and oliguria, cardiotoxicity with hypotension, tachycardia and tachypnea, and CNS

manifestations, including dizziness, headache, convulsions, lethargy, stupor, and coma. Similar are the cases with cobalt and nickel.

MATERIALS AND METHODS

All the reagents used in this work were of analytical grade purity and were used without further purification. All weighing were carried out using Shimadzu TX223L analytical balance, while spectrophotometric measurements were obtained on UV-Visible Spectrophotometer. 0.1M $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ and $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ were prepared in a 100cm^3 volumetric flask each. Similarly, 0.1M solution of L-Dopa was prepared in 100cm^3 volumetric flask. The stoichiometric ratio of M(II) to ligand in the complexes were determined by Job's continuous variation method. Series of volumes (1cm^3) of the 0.1M of M(II) solutions were pipetted into four 50cm^3 volumetric flasks and aliquot (2cm^3) of the 0.1M ligand were added, keeping the mole fraction of the solution constant. The absorbances of each of the solution was taken at the wavelength of maximum absorbance of the complex which was initially determined by varying the wavelengths from 200-400 – 800nm. The procedure was repeated for each of the mole fractions of the complex at various pH ranges and the respective absorbances were recorded at the point of mixing.

UV-vis measurements

The optical densities of some metal-complexes were measured by UV-vis spectrophotometry at specific pH values. The UV-visible spectra were taken using a Shimadzu SP65 UV Visible spectrophotometer in 200-800 nm range using a 1.0 cm quartz cell pathlength at a controlled temperature of $25 \pm 0.1^\circ\text{C}$ with a Cole-Parmer bath.

pH measurements

The pH of the solutions was determined with a Mettler-Toledo MP230 pH-meter provided with a combined electrode (Corning 476086) for pH measurements in the 0–14 pH range. The pH was corrected by taking in account the cell efficiency [39-41] with NaOH at ionic strength 0.5M controlled with NaCl.

RESULT AND DISCUSSION

Typical spectrophotometric parameters are given in Table 1. The absorption of spectra of the ligand and metal ions separately are given in Fig. 1. The absorption spectra of metal-ligand complexes at various pH values are given in Figs. 2-4.

Table 1: Parameters of Co(II), Ni(II) and Cu(II) – L-dopa complexes in different pH ranges.

	Co			
pH	1.65	3.01	5.01	7.50
λ_{max} (nm)	520	520	520	520
Abs	0.088	0.042	.370	0.193
	Ni			
pH	1.80	2.55	4.81	5.54
λ_{max} (nm)	400	400	400	400
Abs	0.042	0.061	0.050	0.075
	Cu			
pH	1.87	2.56	3.01	5.02
λ_{max} (nm)	390	390	390	390
Abs	0.003	0.004	0.013	0.014

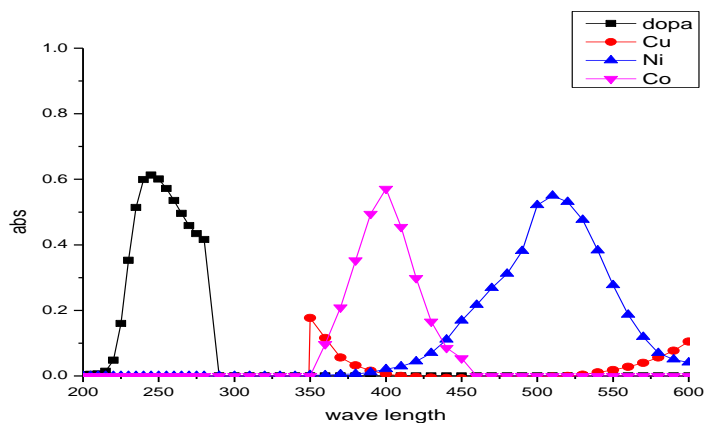


Figure 1: Individual absorption spectra of ligand and metals [dopa, Co(II), Ni(II) and Cu(II)]

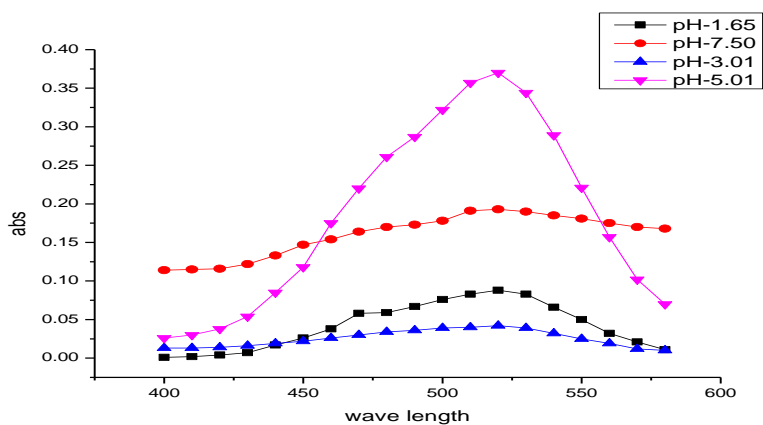


Figure 2: Absorption spectra of Co(dopa)

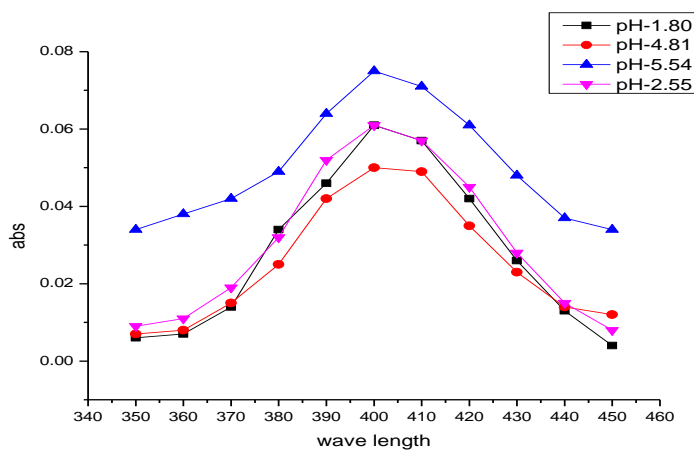


Figure 3: Absorption spectra of Ni(dopa)

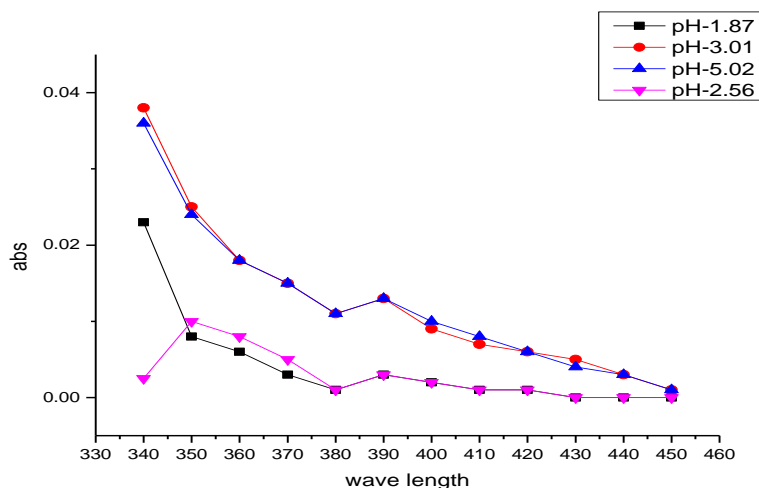


Figure 4: Absorption spectra of Cu(dopa), 1:2 metals to ligand ratio

Job's Method of Continuous Variation

The stoichiometric composition of the coordination compound is determined using Job's continuous variation method. The method consists of mixing equimolar solutions of metal and ligand in varying proportions in such a manner that the total concentration of the metal and the ligand is constant in the resulting mixtures. The absorbance of a series of mixtures is measured at a suitable wavelength. If x mole/liter of L are added to $(1 - x)$ mole/liter of M and if C_1 , C_2 and C_3 are the equilibrium concentrations in moles/liter of M, L and ML_n , respectively, the following relations hold good

$$C_1 = (1-x) - C_3$$

$$C_2 = x - nC_3$$

$$C_3 = C_1 \cdot C_2^n$$

The number of L's (n) attached to metal ion can easily be determined from the position of the maximum or minimum in the graph. If the complex species are coloured and the metal ion and the ligand are colourless, the plots of absorbance versus composition will give a maximum at the composition of the complex. Job's method is ordinarily applicable to systems in which only one complex is present. Gould and Vosburgh [42] have, however, shown that even if a second equilibrium exists in addition to the main reaction, Job's condition is obeyed. The method is applicable to systems which obey Beer's Law.

The stoichiometric composition of the complex is found to be 1:2 (metal: ligand) in all the Co(II), Ni(II) and Cu(II) L-Dopa chelate complexes (Fig. 5).

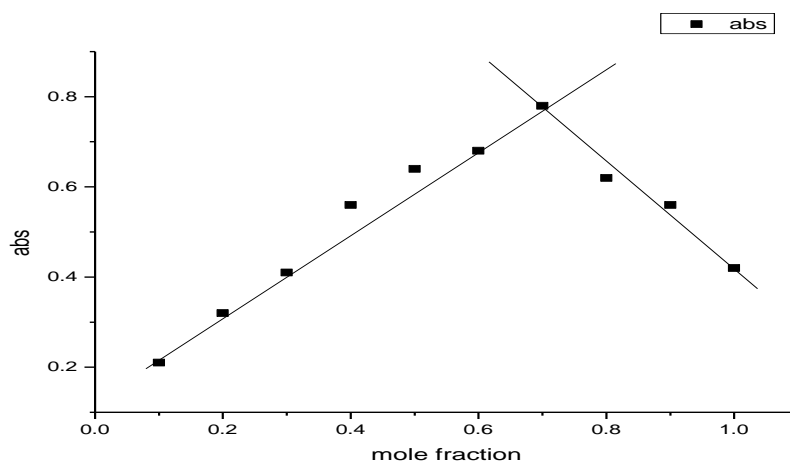


Figure 5: Mole Ratio Determination (Job's Method) for Co(II)-L-Dopa complex

Calculation of Stability Constants

The formulae of highly colored complex ions can be determined in solution using spectrophotometric techniques. Consider the formation of coordination complex $[ML_n]^{z+}$ from a metal ion M^{z+} and a ligand L (Eq. 1):



Assuming that no other species in solution is absorbing radiation of a particular frequency, the Beer - Lambert law (Eq. 2) can be used to calculate the concentration of the complex ion:

$$A_{obs} = [\epsilon_M c_M + \epsilon_L c_L + \epsilon_{ML_n} c_{ML_n}] l \quad (2)$$

A_{obs} = total absorbance of all species in solution

l = pathlength of the cell (taken as 1 cm in this experiment)

$\epsilon_M, \epsilon_L, \epsilon_{ML_n}$ = molar extinction coefficients of the absorbing species

c_M, c_L, c_{ML_n} = concentration of the absorbing species

The conditional stability constants of the complexes were determined from Job's curves Fig 2. Optical density of solution prepared by taking a large excess of ligand (metal to ligand ratio) can be considered as first approximation, to be due to the complex. Knowing the optical density, one may determine values for the extinction coefficient of the complex with the help of Beer's Law. From this value, it is possible to calculate the concentration of the complex in various mixtures and obtain the value of stability constant [43]. The conditional stability constants of a complex can be determined from Job's curves. The two methods usually adopted are as follows

From Extinction Coefficient Data

Optical density of solution prepared by taking a large excess of ligand (metal to ligand ratio 1:2) can be considered as first approximation, to be due to the complex. Knowing the optical density, one may determine values for the extinction coefficient of the complex with the help of Beer's Law. From this value, it is possible to calculate the concentration of the complex in various mixtures and obtain the value of stability constant.

Method of Corresponding Solutions:

A solution containing metal and ligand in 1:2 ratio can be diluted at constant ionic strength, until solutions are obtained having the same optical densities (correction for the absorption for the metal and ligand is made) as those at other ratios. In this manner pairs of solutions may be prepared which have the same optical density (from the complex) and thus contain equal concentrations of the complex but different total concentrations of the metal and ligand.

If D_1 and D_2 are two such values which represent the concentrations $[ML]_1$ and $[ML]_2$ respectively obtained from the observed solutions (i) and (ii) and since $D_1 = D_2$ we may write $[ML]_1$ and $[ML]_2$ and the formation constant K' for this reaction is given by

$$K' = \frac{\{[ML]_1\}}{\{[M]_1 [L]_1\}} = \frac{\{[ML]_2\}}{\{[M]_2 [L]_2\}}$$

Since

$$[ML]_1 = [ML]_2 = [ML]$$

$$K' = \left\{ \frac{[ML]}{T_{M1} - [ML] T_{L1} - [ML]} \right\}$$

$$= \left\{ \frac{[ML]}{T_{M2} - [ML] T_{L2} - [ML]} \right\}$$

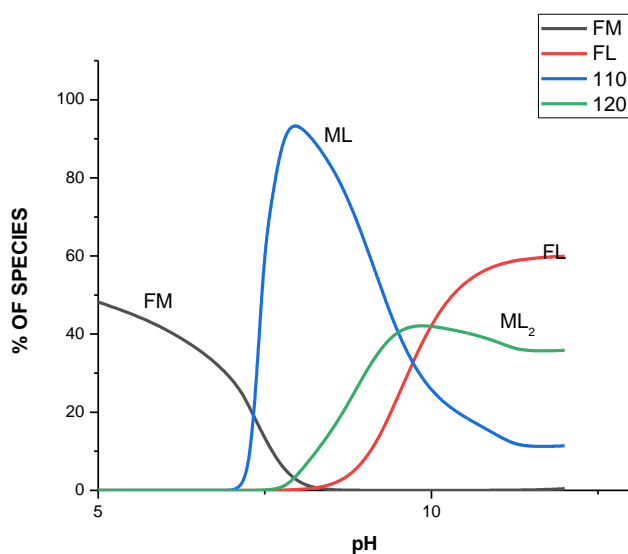
where T_{M1} and T_{L1} correspond to the concentrations of total metal and total ligand respectively in solution (i) and T_{M2} and T_{L2} , correspond to the concentrations of total metal and total ligand, respectively in solution (ii). As the values of T_M and T_L are known, the above equation can be solved to obtain the value of K . The real stability constant K has been shown to be related to the conditional stability constant K' by the following expression proposed by Banks and Singh [43].

$$\text{Log } K = \text{Log} \left\{ \frac{[H^+]^2}{K_1 \cdot K_2} + \frac{[H^+]}{K_2} \right\} \cdot K'$$

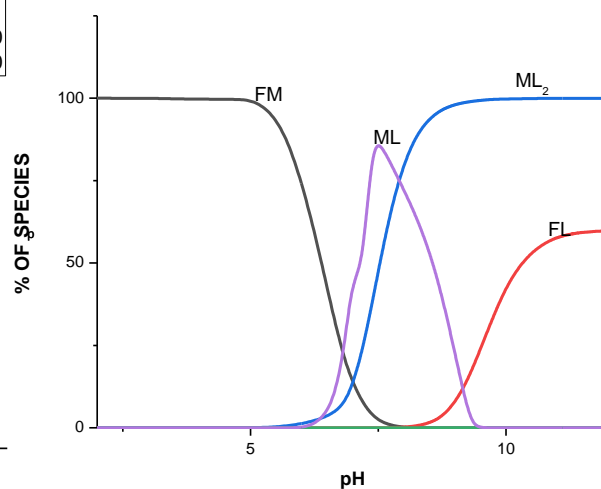
In this expression $[H^+]$ represents the hydrogen ion concentration of the solution, K_1 and K_2 are the first and second dissociation constants of the ligand acids

Table 2: Stability constants of L-Dopa complexes with Co(II), Ni(II) and Cu(II)

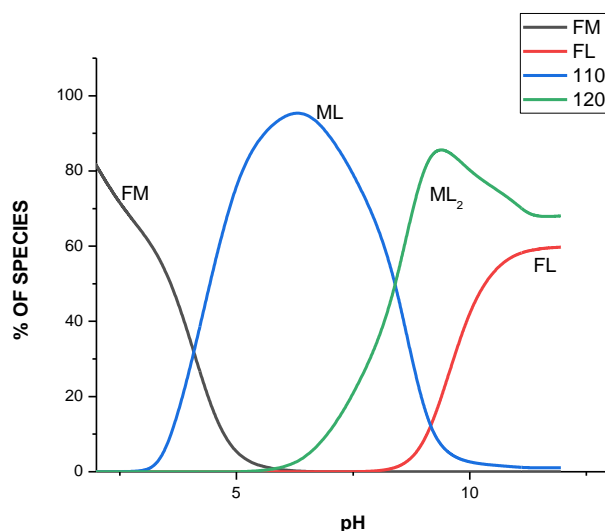
Metal	Log K_{MLH}	
	110	120
Co(II)	5.84	8.69
Ni(II)	7.19	10.53
Cu(II)	11.98	16.13



(a)



(b)



(c)

Figure 6: Distribution diagrams of binary complexes of L-Dopa in 1:2 metals to ligand ratio (a) Co(II), (b) Ni(II) and (c) Cu(II).

STRUCTURES OF COMPLEXES

When the second donor site of L-Dopa is a nitrogen atom, marked bidentate behavior is frequently found, more so when the additional chelat-ion results in a five or six membered ring. Octahedral structures are proposed to the complexes of all the metal ions.

The VSEPR theory suggests that Co(II), Ni(II) and Cu(II) complexes shall be octahedral because there are six outer electron pairs. Amino nitrogen atoms can associate with hydrogen ions in physiological pH ranges. Hence, there is often significant competition between hydrogen and metal ion for this second donor site. This situation results in the simultaneous existence of a number of equilibria producing an array of successively protonated complexes. Hence, protonated complex species are detected in the present study. Amino nitrogen and carboxyl oxygen of L-Dopa participate in bonding with metal ions[44]. Based on the above arguments, depending on the active sites in the ligand and nature of metal ions, the structures were proposed for the species detected are as shown in the Fig. 7.

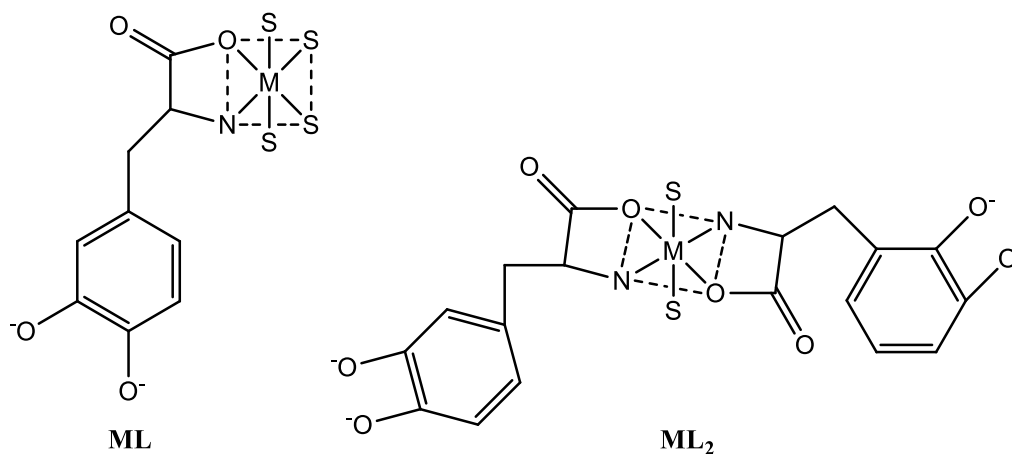


Figure 7: Structures of L-dopa complexes, where S is either solvent or water molecules.

CONCLUSIONS

Complexes resulting from the coordination of the metal ions with the chelating ligand (L-Dopa) are stable at different pH ranges, a property which accounts for the numerous applications of the complexes.

- L-Dopa forms both protonated and unprotonated complexes under a pH range of 2.0-11.0.
- Due to the interaction of L-Dopa with metals Co(II), Cu(II) and Ni(II), the binary species ML, ML₂ are formed. These models are validated by using statistical treatment of the data.
- The order of ingredients influencing the magnitudes of stability constants due to incorporation of errors in their concentrations is alkali > acid > ligand > metal.
- Dopa is ambidentate ligand and it can bind through either amino acid side chain or phenolic groups depending on pH.

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