Electrochemical and Computational Study of Copper Histidine Complex via Cyclic Voltammetry

[1]Atya Hassan*, [1]Sana Gul, [2]Taswar Ali Chandio and [3]Muhammad Ali Minhas
[1]*Federal Urdu University of Arts, Science and Technology, Gulshan-e-Iqbal Campus Karachi, Karachi, Pakistan. 75300.*
[2]*Department of Chemistry, Faculty of Science, Gazi University Ankara, 06500, Turkey.*
[3]*International Center for Chemical and Biological Sciences, H.E.J. Research Institute of Chemistry, University of Karachi, Karachi, Pakistan.*
atya007chem@gmail.com*

(Received on 21st June 2021, accepted in revised form 6th January 2022)

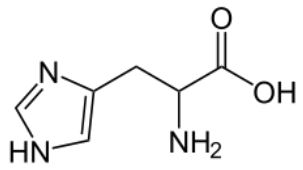
Summary: L-Histidine regulates body function and involve in the synthesis of hemoglobin, repairing of tissues and strengthens of immune system. In this study, Cyclic Voltammetry (CV) is used with 0.1 M Potassium Chloride as a supporting electrolyte to determine the accurate metal ligand ratio between Cu^{+2} and L-Histidine. In CV potential window is set between +0.6 to -0.4V to record the Voltammogram. Voltammograms were recorded by varying scan rate from 50mV/s to 300mV/s. Cyclic Voltammetry is used to analyzed the interfacial performance of the complex and repeated Cyclic Voltammograms (07 cycles) were recorded at Glassy Carbon Electrode (GCE), that shows no change in peak current intensity of both anodic and cathodic peak. Further, neither pre nor any post peak was observed. These interpretation express that reactant and product are not involve in the adsorption-desorption process at the surface of Glassy Carbon Electrode (GCE). These remarks suggest that it is diffusion controlled process in the above mentioned system. The interaction of Cu^{+2} and L-Histidine were not reported before through Cyclic Voltammetry. Furthermore, in this study structure of Cu^{+2} vs. L-Histidine complex is investigated from a theoretical perspective. Optimization of Cu^{+2} vs. L-Histidine complex was carried out by DFT method and result verifies that stable structure of Cu^{+2} vs. L-Histidine complex exist as square planar structure in 1:2 ratio respectively. The computed structure has correlation with experimental results and Voltammogram of 1:2 ratio complex of Cu^{+2} vs. L-Histidine suggested that it exist in Square planar geometry.

Keywords Cyclic Voltammetry (CV), Glassy Carbon Electrode (GCE), Density Functional Theory (DFT), Saturated Calomel Electrode (SCE), L-Histidine.

Introduction

Electrochemistry is the better path way to explain the interaction of metal ion with biologically active compound. Recently, usage of metal ligand complexes increases in medicinal chemistry for therapeutic purpose [1, 2]. It is required in normal functioning of plants, animals and most microorganisms used in specific metabolic functions. The copper has various biological importance including regulation of hemoglobin, embryonic development, hepatocyte and neuronal functions, where it also has environmental importance like mitochondrial respiration [3]. Being a transition metal, Cu (metal) has capability to change their oxidation states between two different redox states i.e. oxidized Cu^{+2} and reduced Cu^{+1}. It also involves in many catalytic processes as a co-factor and involve in metabolic reactions of biological systems. Generally copper has been reported as antibacterial, antiplaque agent in mouth washes and toothpastes. It is also used to control the growth of unnecessary organisms in fish farming. It is antifouling agents used on fish net and have been considered as a source of metal to the sediments [1, 4].

L-Histidine is one of the semi-essential amino acid and it is typical an aromatic amino acid [5-7]. The (S)-2-Amino-3-(4-imidazolyl)propionic acid is IUPAC name of L-Histidine and molecular formula is NH-CH=N-CH=C-CH_2-CH(NH_2)-COOH. It contains two basic and one carboxylic acid group. An alkyl group (R) occupies an imidazole ring which is shown in (Scheme-1) [8]. The imidazole group of L-Histidine is basic in nature. It is involved in several metabolic reactions and also involve in formation of proteins in human body [9, 10].



Scheme-1: Structure of L-Histidine.

Literature review reveals that the reduction of Cu^{+2} was reported at different pH in presence of various ligands such as Thymine, Aspartic acid, L-

*To whom all correspondence should be addressed.

Phenyl alanine, Ascorbic Acid, L-Leucine, Norfloxacin, DNA, and Guanine through electrochemical process [11-19]. Different parameters such as kinetic behavior and reduction of Cu^{+2} have been examined using several techniques such as AC polarography, electrochemical behavior, DC polarography [20-25], Coulometry, Chronoamperometry with constant potential and Hydrodynamic Voltammetry [26, 27]. Various results concluded that the Cu^{+2} forms very stable complex with serine but potentiometric studies showed that Cu^{+2} serine complex is not stable due to the presence of $-NH_3^+$. Till date no research work is reported for the interaction of Cu^{+2} with L-Histidine by Cyclic Voltammetry. In addition, computational resources have been used to elucidate geometry of complex that remained unsolved for decades.

Experimental

Preparation of $CuCl_2$ and L-Histidine solution

The equimolar solution of $CuCl_2$ (E. Merk) (0.0333 M) and L-Histidine (E. Merk) (0.0333 M) solutions were prepared in 20 mL and 50 mL volumetric flask respectively by using (0.1M) KCl solution as a supporting electrolyte because KCl inhibit the direct migration of analytes towards the working electrodes from bulk of the solution. Cyclic Voltammeter (CHI-700d) is accessible in Department of Chemistry Fuuast was used for the measurements of potential of the complex at 302K. This instrument consists of three electrodes *i.e.* GCE, Saturated Calomel Electrode (SCE) and Platinium wire (Pt) were used as a working, reference and counter electrode respectively. Good current response was observed in GCE instead of metallic electrode due to this reason GCE was use in this experiment The electrochemical range starts from +0.6 and recorded till -0.4 V. Initially, base line has been recorded which is horizontally straight and after that by varying scan rates between 50mV/s to 300mV/s Voltammograms were recorded. Finally for estimation of adsorption behavior repetitive cycles were recorded.

Computational Set up

For quantum calculations Guassian 09 package [28] has been used. Initially Cu^{+2} -L-Histidine complex was built at Gauss View program [29]. For optimization of Cu^{+2}-L-Histidine complex Density Functional Theory (DFT) was used with B3LYP method as most popular function. In this study, 6-31 G (d,p) basis set was used to estimate optimize structure to the minima on the potential surfaces. Further thermodynamic parameter i.e. Energy was estimated.

Results and Discussion

In present work the electrochemical response of L-Histidine is recorded with 0.1M KCl and only one broad peak appeared in the range of -0.1V to -0.3V (Fig. 1). It is observed that neither oxidation nor reduction peak appeared in both forward and reverse cycle. The result suggested that free ligand (L-Histidine) neither undergo redox process at surface of GCE. Similarly the Voltammogram of Cu^{+2} solution was also recorded within same potential range with 50 mV/s scan rate (Fig. 2). Voltammogram of Cu^{+2} showed Ipc^1 (Peak 1) and Ipc^2 (Peak 2) as two cathodic peaks in forward scan. The Ipc^1 peak expressed Cu^{+2} undergo reduction with gain of one electron into Cu^{+1} while the Ipc^2 peak showed further reduction of Cu^{+1} into Cu^o metal. It is shown in equation (1 and 2).

$$Cu^{+2} + 1e^- \rightarrow Cu^{+1} \quad (1)$$

$$Cu^{+1} + 1e^- \rightarrow Cu^o \quad (2)$$

Likewise, two intense anodic peak Ipa^3 and Ipa^4 were found. The peak Ipa^3 indicate the removal of single electron from the copper metal i.e. Cu (0) to Cu (+) where Ipa^4 reflects the further oxidation of Cu^{+1} into Cu^{+2} [4, 24]. It is shown in equation (3 and 4)

$$Cu^o \rightarrow Cu^{+1} + 1e^- \quad (3)$$

$$Cu^{+1} \rightarrow Cu^{2+} + 1e^- \quad (4)$$

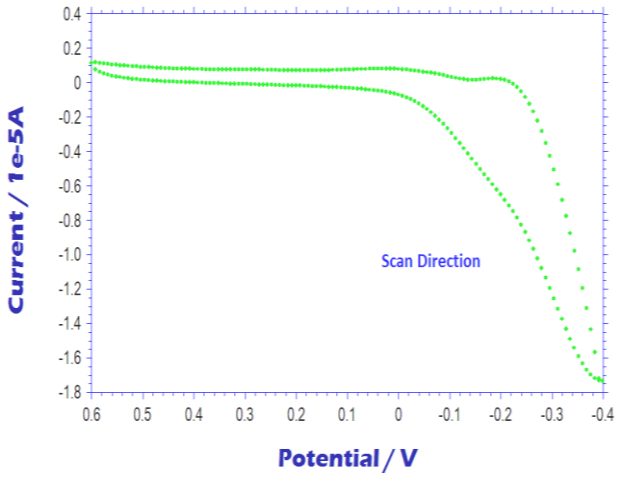


Fig. 1: Cyclic Voltammogram of (5mM) Histidine in (0.1M) KCl solution as a supporting electrolyte at 50mV/S scan rate at temperature of 305±1K at GCE.

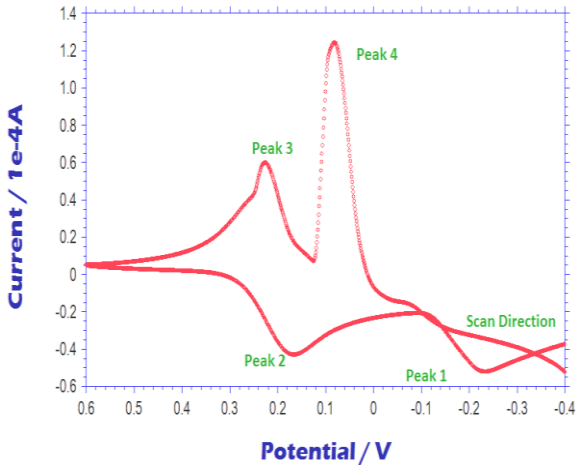


Fig. 2: Cyclic Voltammogram of 5mM Cu (II) solution at the scan rate of 50mV/s in 0.1M KCl at GCE at the temperature = 305±1K.

Effect of the different ratio of ligand (L-Histidine) on the Voltammogram of Cu^{+2} metal

The complex formation between Cu^{+2} and L-Histidine was studied by Cyclic Voltammetry techniques. In this method, different concentration ratio of L-Histidine such as (1ml, 2ml, 3ml, 4ml and 5ml) were used. It was noticed that the anodic and cathodic peak was gradually shifted by increasing the volume of ligand. The shifting of peak position gave the positive response to the formation of Cu^{+2} -L-Histidine complex.

1:1 ratio Cu^{+2} + L-Histidine vs. Cu^{+2}

Overlay of Cyclic Voltammogram of Cu^{+2} and metal Ligand mixture (ratio 1:1) showed clear difference to the shifting of peak (Fig.3). The Voltammogram of (metal+ligand) solution (B) revealed that Epa^4 (Peak 4), Epc^1 (Peak 1) get shift to more where Epc^2 (Peak 2), Epa^3(Peak 3) became a slightly move towords more negative potential as compared to Voltammogram (A) (Fig. 3). In case of Voltammogram (B), all peaks suppressed vertically and show changes in current with comparion of Voltammogram (A).

When the Cu^{+2} reduced into Cu^o electron transfer couple became less intense as compare to the Peak Ipc^1 for the reduction of Cu^{+2} to Cu^{+1}. The above mentioned process explained that the stability of Cu^{+2} and Cu^{+1} ions retained in aqueous solution due to the hydration energy of the copper ions with bounded water molecules. Charge density of the Cu^{+2} ion found to be greater due to smaller in size as compare to Cu^{+1} ion due to this reason Cu^{+2} ions make stronger bond as a result releasing more energy. In non-aqueous medium Cu^{+1} is found to be stable in presence of ligand such as Cl^- [4]. However, Cu^{+2} ions surrounded loosely with solvent molecules than Cu^{+1} ions. In reverse scan, Cu^o get oxidized into Cu^{+1} and then into Cu^{+2} showing change in peak current of Ipa^3 (Peak 3) and Ipa^4 (Peak 4) respectively. It is inferred that during forward scan the specie which is formed by Cu^{+1} showed less intense peak Ipc^2 and unstable at GCE in KCl medium.

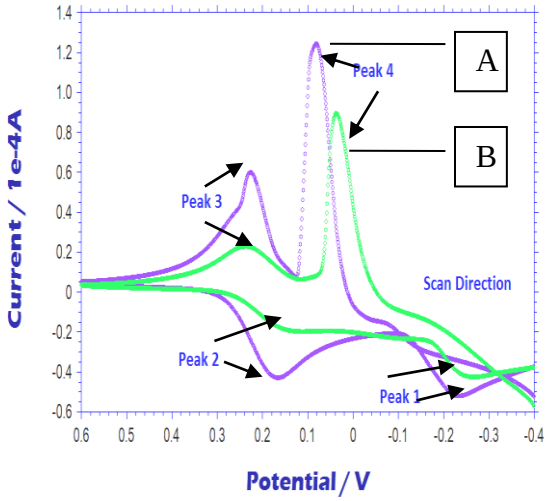


Fig. 3: (A) Cyclic Voltammogram of Cu (II) solution 5mM and (B) Cu (II)+L-Histidine solution 1:1 metal to ligand ratio at the scan rate of 50mV/s in 0.1MKCl solution at temperature = 305±1K.

1:2 ratio Cu^{+2}+L-Histidine vs. Cu^{+2}

Further, in copper solution twice volume of L-Histidine was used (1:2 ratios). In Voltammogram only one anodic peak (Ipa^4) was obtained and all cathodic peaks were vanished (Fig. 4). The peak Ipa^4 showed an oxidation of Cu^{+1} into Cu^{+2} for pure copper solution (i.e. without ligand), where in metal-ligand complex (1:2) this peak shows peak current of 30.18µA to 73.34µA, which is less than pure copper solution (ranging 124.6µA to 338.6µA) and also lesser than Cu^{+2}-L-Histidine (1:1) complex ratio (ranging 89.35µA to 280.6µA). It is inferred that increase in ligand ratio decreases intensity of the anodic peak's where peaks potentials are also shifting to lesser values as shown in (Table-1).

Table-1: Values of Peak separation and ratio of peak current of 1:1 metal to ligand ratio of Cu (II)+L-Histidine solution and 5mM Cu (II) solution at 50 to 300 mV/s in 0.1M KCl solution as a supporting electrolyte at temperature = 305 ±1K.

Scan Rates (mV/s)	Cu–L-Histidine solution (1:1)		Copper solution	
	Epa^4-Epc^1 (V) (-)	Ipc^1/ Ipa^4(-)	Epa^4-Epc^1 (V)(-)	Ipc^1/ Ipa^4(-)
50	0.231	0.480	0.153	0.424
100	0.240	0.399	0.170	0.381
150	0.472	0.367	0.323	0.363
200	0.263	0.344	0.166	0.357
250	0.260	0.329	0.166	0.372
300	0.523	0.314	0.332	0.388

1:3 ratio Cu^{+2} + L-Histidine vs. Cu^{+2}

Further addition of 3 ml of Ligand in Cu^{+2} solution (volume of metal solution kept constant), no change was found in the shape of Voltammogram of metal ligand complex as compared to 1:2 ratio of metal ligand complex Voltammogram. For 1:3 metal ligand Voltammogram peak 4 was found to be suppressed (Fig. 5). Although Voltammogarm of Cu^{+2} contained well defined two anodic and two cathodic peak. Similar to 1:2 metal ligand complex the anodic peak intensity decreases with the increase of ligand ratio and also the peak potential are also shifted to lesser values as shown in the (Table-1).

1:4 and 1:5 ratio Cu^{+2} + L-Histidine vs. Cu^{+2}

An interesting result was perceived in the Voltammogram of Copper ligand solution of 1:4 and 1:5 ratio, metal to ligand ratio in both cases (B), showing oxidation of a complex. The only one anodic peak was obtained and cathodic peaks were disappeared completely (Fig. 6 and 7).

Quantum Theoretical analysis

Initially geometry of transition metal complex is optimized to a local minimum; it has been difficult to converge large molecules to its minimum. Cu-L-Histidine (1:2) ratio was optimized via DFT along with B3LYP method and 6-31G basis set was used. The geometry optimization step is depicted in Fig. 8 The detailed coordinates of start and converged geometry is shown in Table-4. It is investigated that during optimization of Cu-L-Histidine (1:2) ratio complex, it remains stable and didn't showed failure during convergence to local minimum. It further confirms that Cu-L-Histidine (1:2) ratio complex showing cathodic peak in cyclic Voltammetry and showed formation of complex with stability. Further to check thermodynamic stability of complex, binding energy was calculated to confirms the stability of complex, so for Cu-L-Histidine complex binding energy is -1.1928 $x10^{-1}$ Kcal, hence negative binding energy confirms the stability of complex.

Suggested structure of Copper- L-Histidine

Voltammogram of the Cu^{+2} (Fig.1) showed two anodic and two cathodic peaks while L- Histidine (Fig.2) expressed just only one broad peak. But the Voltammogram of 1:1 ratio solution of [Cu^{+2} +L-Histidine] did not indicated the significant change in Voltammogram just peak size and position were shifted (Fig. 3). When the L-Histidine ratio become twice the significant change was percived as the result peak 1, peak 2 and peak 3 vanished only peak 4 persist (Fig. 4). However, the peak current of Cu^{+2} suppressed when the L-Histidine ratio increases.

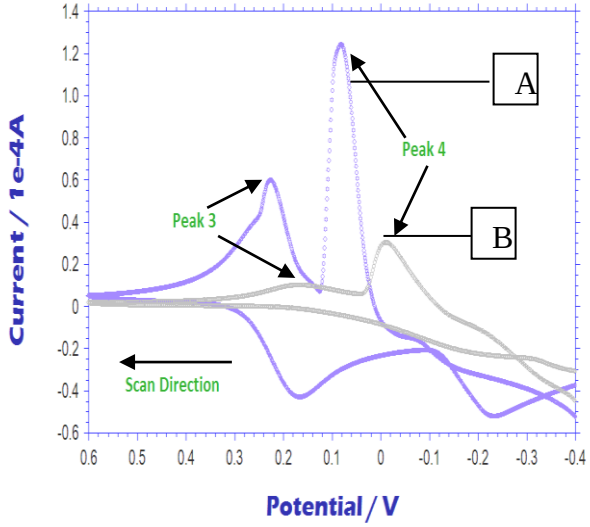


Fig. 4: (A) Cyclic Voltammograms of 5mM Cu (II) solution and (B) Copper-L-Histidine solution with 1:2 metal to ligand ratio taken at 50mV/s in 0.1M KCl solution at temperature = 305±1K.

It is concluded that changes occur in Voltammogram with different metal ligand ratio and the proposed structure could be histamine like coordination (Scheme-2) [15, 30-32]. It has been validated histamine like coordination of Cu-L-Histidine complex is stable during optimization by DFT method. So Cu-L-Histidine complex exist as square planar and Histidine acts as a bi-dentate ligand coordinating with Copper metal via N-terminal amino acid and N-atom of imidazole ring of L-Histidine.

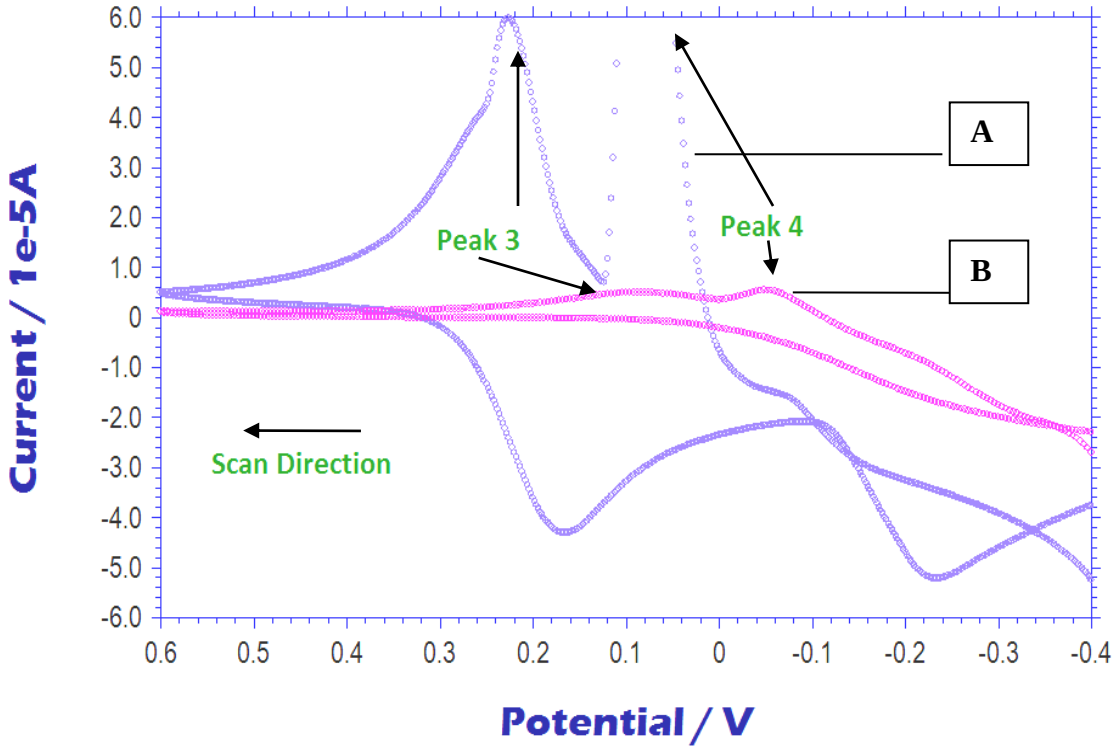


Fig. 5: (A) Cyclic Voltammograms of 5mM Cu (II) solution and (B) Cu (II)-L-Histidine solution with1:3 metal to ligand ratios at the scan rate of 50mV/s in 0.1M KCl solution at temperature = 305±1K.

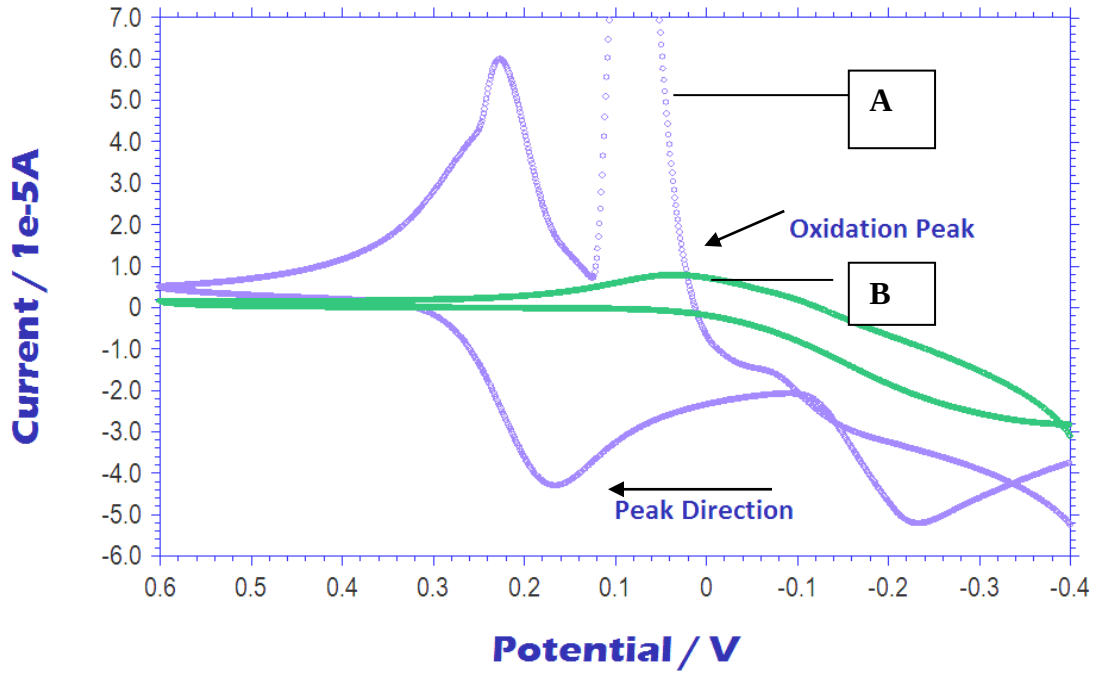


Fig. 6: (A) Cyclic Voltammograms of 5mM Cu (II) solution and (B) Cu (II)-L-Histidine solution with 1:4 metal to ligand ratios at 50mV/s scan rate in 0.1M KCl solution as a supporting electrolyte at temperature= 305±1K.

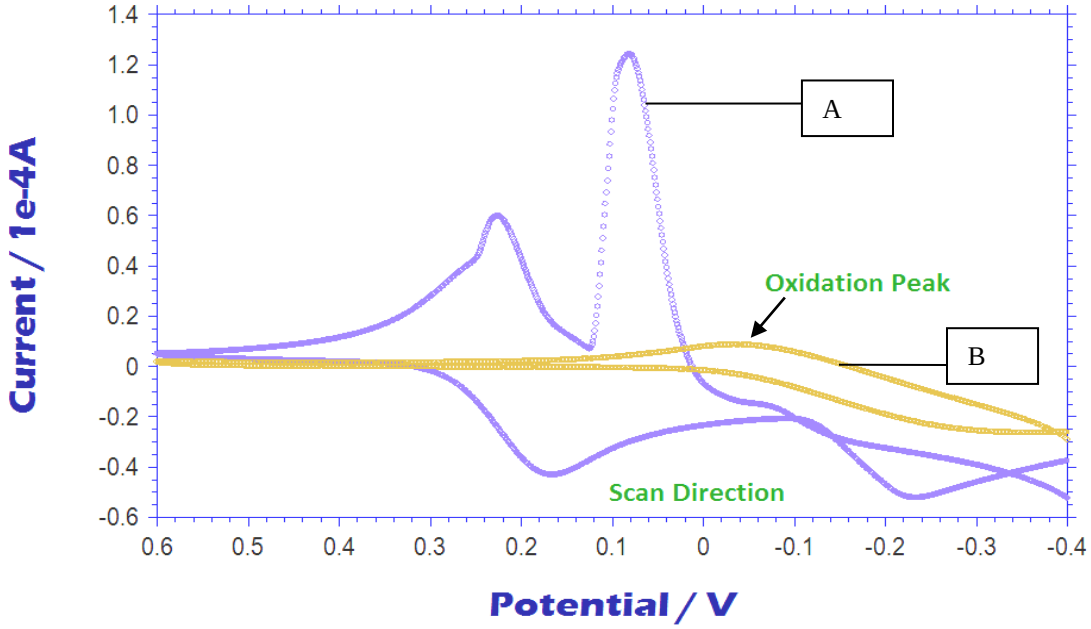


Fig. 7: (A) Cyclic Voltammograms of 5mM Cu (II) solution and (B) Cu (II)-L-Histidine solution with 1:5 metal to ligand ratio at the scan rate of 50mV/s in 0.1M KCl solution at temperature = 305±1K.

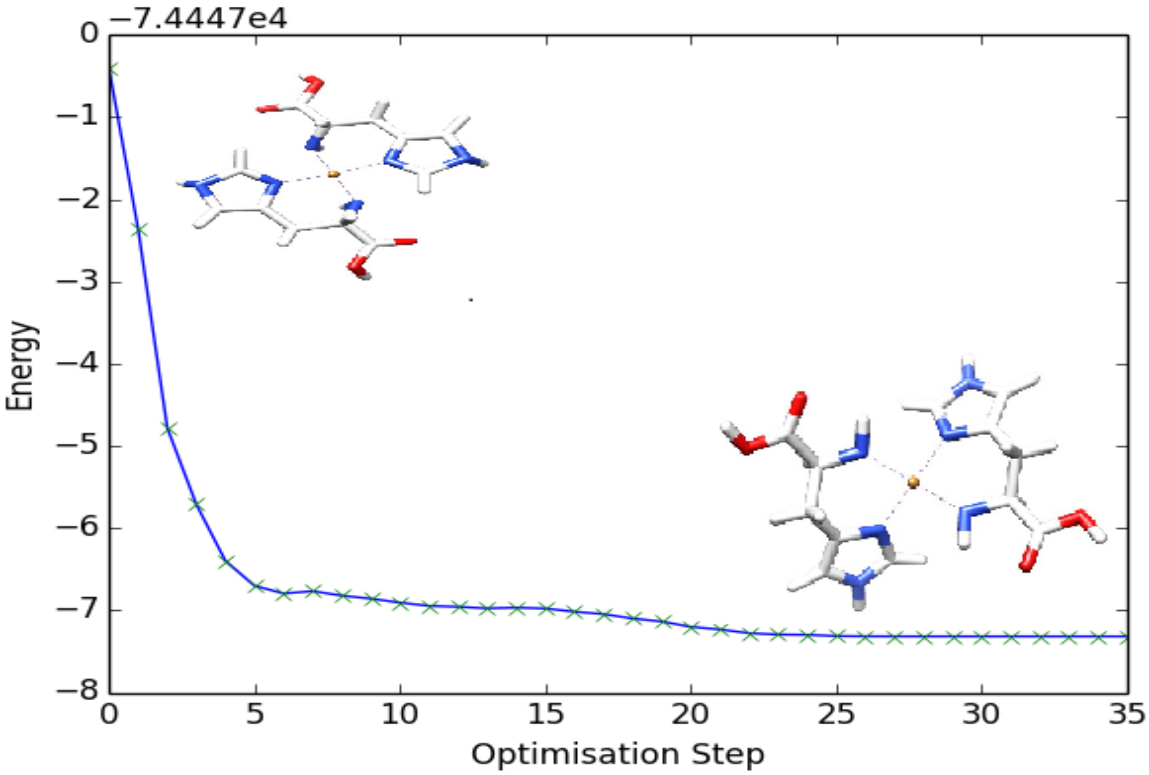


Fig. 8: Optimization of Cu (II)-L-Histidine (1:2) ratio complex via DFT method along with Energy and optimization step of geometry complex.

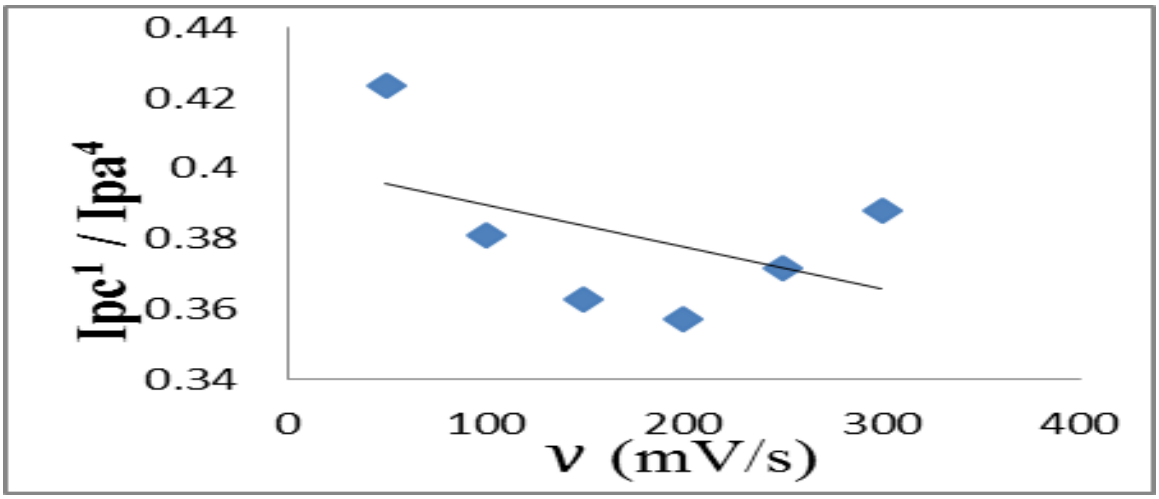


Fig. 9: A plot showed variation in peak current ratio (Ipc^1/ Ipa^4) with scan rate (v) from 50mV/s to 300mV/s for cyclic Voltammogram of pure Copper solution in 0.1M KCl solution as a supporting electrolyte.

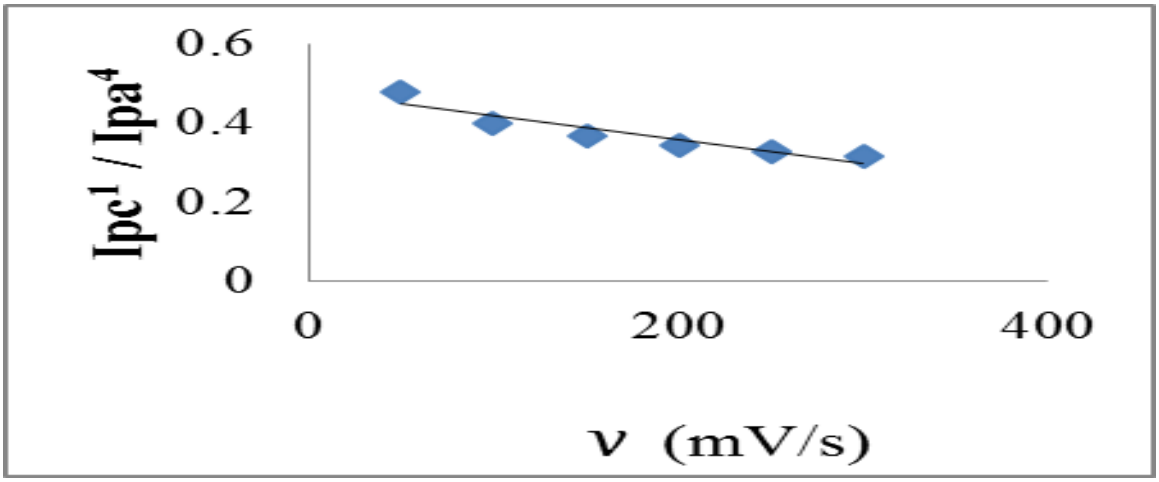
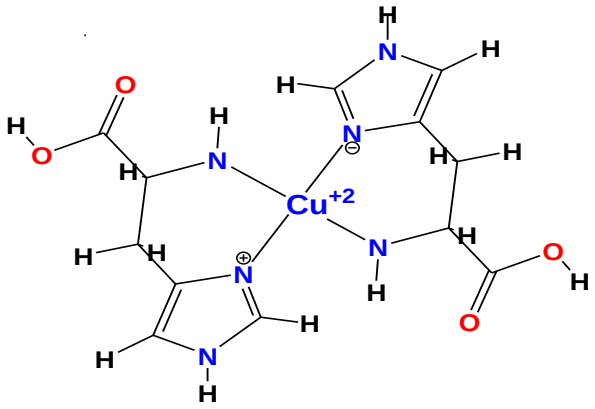


Fig. 10: A plot showed variation in peak current ratio (Ipc^1/ Ipa^4) with scan rate from 50mV/s to 300mV/s for cyclic Voltammogram of Copper (II)-L-Histidine solution with 1:1 metal to ligand ratio in 0.1M KCl solution as a supporting electrolyte.



Scheme-2: Suggested structure of [Cu^{+2} -L-Histidine].

Table-2: Cyclic Voltammetry data obtained at GCE corresponding to the reduction process of Copper-L-Histidine solution with 1:1 metal to ligand ratio at scan rates from 50mV/s to 300mV/s in 0.1M KCl solution as a supporting electrolyte.

Scan Rate(mV/s)	Cathodic peak						Anodic Peak			
	Epc^1(V)(-)	Ipc^1(μA)(-)	Epc^2(V)	Ipc^2(μA)(-)	Epa^3(V)	Ipa^3 (μA)	Epa^4(V)	Ipa^4(μA)	Epa^4-Epc^1(V)(-)	Ipc^1/ Ipa^4(-)
50	0.268	42.84	0.135	19.60	0.238	22.68	0.037	89.35	0.231	0.480
100	0.299	55.80	0.102	25.53	0.242	37.80	0.059	139.8	0.240	0.399
150	0.328	65.18	0.074	28.44	0.250	52.08	0.065	177.8	0.472	0.367
200	0.335	73.24	0.076	31.30	0.255	65.76	0.072	213.1	0.263	0.344
250	0.338	81.60	0.078	34.37	0.262	77.62	0.078	248.3	0.260	0.329
300	0.342	87.97	0.050	37.29	0.267	90.80	0.085	280.6	0.523	0.314

Table-3: Cyclic voltammetry data obtained at GCE corresponding to the reduction process of Copper-L-Histidine solution with 1:1, 1:2 and 1:3 metal to ligand ratio at scan rates from 50mV/s to 300mV/s in 0.1M KCl solution as a supporting electrolyte.

No. of Sample	Cathodic peak potentials		Cathodic Peak Currents		Anodic peak potential		Anodic Peak Currents	
	Epc^1(V)	Epc^2(V)	Ipc^1(μa)	Ipc^2(μa)	Epa^3(V)	Epa^4(V)	Ipa^3(μA)	Ipa^4(μA)
Copper	-0.233	0.165	-52.80	-43.49	0.225	0.080	60.21	124.6
Copper +L-Histidine (1:1)	-0.268	0.135	-42.84	-19.60	0.238	0.037	22.68	89.35
Difference	-0.035	0.0030	-9.960	-23.89	0.013	0.043	37.53	35.25
Copper +L-Histidine (1:2)	-	-	-	-	0.153	-0.012	15.39	30.18
Difference	-	-	-	-	0.072	0.092	44.82	94.42
Copper +L-Histidine (1:3)	-	-	-	-	0.088	-0.050	5.058	5.476
Difference	-	-	-	-	0.137	0.130	55.16	119.2

Table-4: Coordinates of Cu (II)-L-Histidine (1:2) ratio before optimization and after optimization by DFT method.

Center Number	Atomi Number	Coordinates (Angstroms) before optimization			Coordinates (Angstroms) after optimization by DFT method		
		X	Y	Z	X	Y	Z
N1	7	-0.70485	1.517425	0.97374	1.55289	0.98083	0.348778
C2	6	-0.2381	2.82063	0.38627	-2.92285	0.56366	0.296
C3	6	-1.04692	3.960087	-1.04667	-3.75671	1.569773	1.132601
C4	6	1.258619	3.098114	-0.63452	-3.08859	-0.92676	0.649468
O5	8	-0.49006	5.272839	-1.14247	-4.94851	1.07995	1.445409
O6	8	-2.21224	3.733435	-1.50339	-3.32513	2.666565	1.397471
C7	6	2.09695	2.033425	0.03401	-2.36318	-1.81863	-0.31261
N8	7	1.658384	0.675992	0.244133	1.05406	-1.57522	-0.72278
C9	6	2.691682	0.009357	0.798983	-0.71257	-2.56227	-1.55413
N10	7	3.923356	0.831945	0.73769	-1.74159	-3.41387	-1.69052
C11	6	3.361572	2.172878	0.49663	-2.79362	-2.9668	-0.92159
N12	7	0.708994	-1.72738	-0.59705	1.553668	-0.98126	0.347865
C13	6	0.328816	-2.78562	0.371841	2.923342	-0.56312	0.295825
C14	6	1.154166	-4.03517	0.012644	3.757532	-1.56889	1.132467
C15	6	-1.22475	-3.14772	0.164946	3.087944	0.92738	0.649469
O16	8	0.588667	-5.33403	0.240926	4.948707	-1.07815	1.446269
O17	8	2.337793	-3.90821	-0.50037	3.326795	-2.66621	1.396505
C18	6	-2.14329	-1.94821	0.415721	2.36248	1.818711	-0.31306
C19	6	-2.76613	0.197714	0.583119	0.711912	2.561121	-1.55537
N20	7	-4.00215	-0.64642	0.69849	1.740618	3.413077	-1.69185
C21	6	-3.44212	-2.00072	0.810161	2.792617	2.966783	-0.92241
H22	1	-0.47224	1.473481	-1.95221	-1.52038	1.989106	0.563284
H23	1	-0.39692	2.809606	0.648308	-3.27702	0.714052	-0.74528
H24	1	1.512376	4.059202	-0.24322	-4.1521	-1.17168	0.644674
H25	1	1.4563	3.09049	-1.70826	-2.73134	-1.08709	1.674207
H26	1	-0.90756	5.744543	-1.85585	-5.45567	1.749857	1.942257
H27	1	2.672489	-0.97161	1.250156	0.232736	-2.67461	-2.06324
H28	1	4.486714	0.535136	-0.04574	-1.74203	-4.24584	-2.26878
H29	1	3.859584	3.102957	0.62256	-3.73432	-3.49271	-0.86851
H30	1	0.361528	-1.99171	-1.52564	1.521837	-1.9897	0.56165
H31	1	0.511655	-2.47995	1.366547	3.278127	-0.71313	-0.74534
H32	1	-1.50232	-3.94687	0.819273	4.151303	1.173004	0.64525
H33	1	-1.37398	-3.45837	-0.87461	2.730051	1.087499	1.674015
H34	1	0.970574	-5.95397	-0.40575	5.456154	-1.74786	1.943087
H35	1	-2.7432	1.252878	0.754607	-0.23331	2.672874	-2.06475
H36	1	-4.54857	0.55655	0.13587	1.740903	4.244776	-2.2705
H37	1	-3.96634	-2.88207	1.117494	3.733112	3.493062	-0.86937
Cu38	29	-0.0182	-0.05862	-0.19244	0.000065	-0.00041	-0.1991
N39	7	-1.74029	-0.55894	0.26154	1.053567	1.5746	-0.72349

Effect of Scan Rate on ΔE andIp^{c}/ Ip^{a}ratio

The ratio of Ipc^{3}/ Ipa ^{1} peak current is about 0.388-0.424V in pure Cu^{+2} where it is about 0.314 - 0.480V in case of Copper L-Histidine complex (1:1) (Table-2). It was observed that by increasing scan rate, the ratio of peak current gets decreases as shown in (Fig. 9 and 10). However, a further Copper L-Histidine ratio from 1:2 to 1:5 was examined and they didn't have this ratio (Ipc^{3}/ Ipa ^{1}) because absence of cathodic peaks.

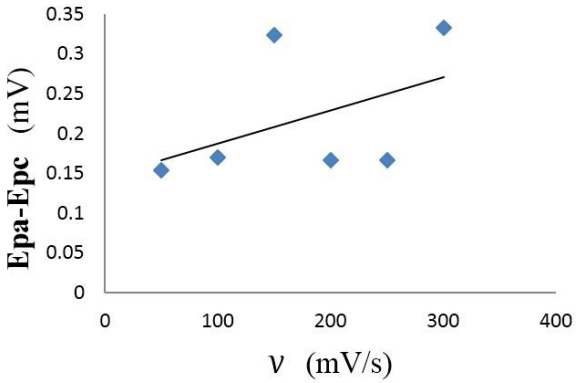


Fig. 11: A plot showed variation in peak potential separation of pure Copper solution at a scan rate from 50mV/s to 300mV/s in 0.1M KCl solution as a supporting electrolyte.

The difference of peak potential values ($\Delta Ep = Ep^{a} - Ep^{c}$) rises gradually by the increasing the scan rate in pure Cu^{+2} and in Copper L-Histidine (1:1) ratio complex (Fig. 11 and 12). Further study shows the different ratio of Copper L-Histidine i.e. 1:2, 1:3, 1:4 and 1:5 may have peak potential separation $\Delta Ep = Epa - (Epa)_{1/2}$ due to complete removal of cathodic peaks. It also increases by increasing scan rate (Fig. 11 and 12). The ranges of ΔE are larger than the theoretical value (0.059 V) for the reversible electron transfer process (Table-3).

It is inferred that this redox reaction is quasi reversible process despite of reversible reaction. It was also observed that separations of peak potentials increases with the uplift of scan rate hence it supports charge transfer kinetics.

Effect of Scan Rate on Anodic Current

The reduction behaviour of Cu^{+2} shows a linear relationship vs. square root of scan rates and it permits through the origin (Fig. 13). This fact shows that this is diffusion controlled process and it also observed that no adsorption takes place on the electrode surface of GCE. Furthermore, results are in good agreement with the previous study.

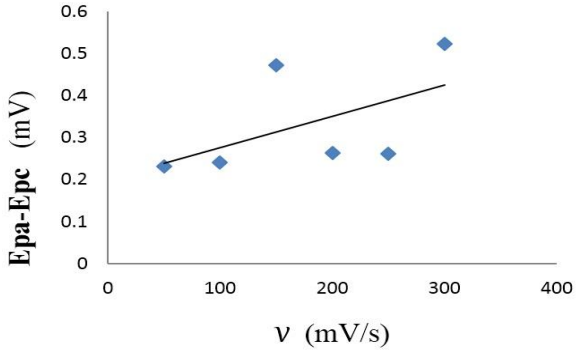


Fig. 12: A plot showed variation in peak current ratio (Ipc1/ Ipa 4) with scan rate from 50mV/s to 300mV/s for CyclicVoltammogram of Cu (II)-L-Histidine solution with 1:1 metal to ligand ratio in 0.1M KCl solution as a supporting electrolyte.

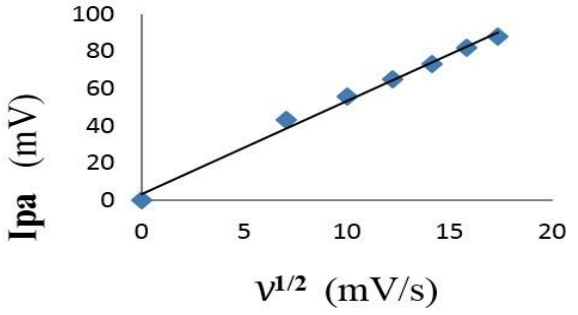


Fig. 13: A plot showed variation of anodic peak current with the square root of scan rate from 50mV/s to 300mV/s for Cyclic Voltammogram of Cu (II)-L-Histidinesolution with 1:1 metal to ligand ratio in0.1M KCl solution as a supporting electrolyte.

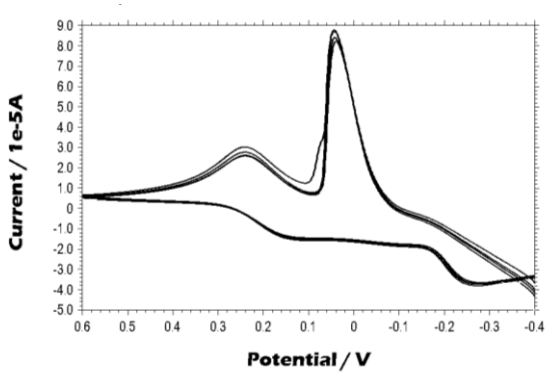


Fig. 14: Repetitive Cyclic Voltammograms at Glassy Carbon Electrode of Cu (II)-L-Histidine solution with 1:1 metal to ligand ratio at scan rate of 50mV/s in 0.1 M KCl as a supporting electrolyte at temperature = 305±1K.

Study of adsorption process

The adsorption behavior of the complex was also evaluated by taking the more than one (07 cycles) Voltammograms at 50mv/S scan rates at GCE electord, which indicates no significant change occur in the intensity of anodic or cathodic peak current. Further observed that there is no pre and post peak in all the Cu^{+2} L-Histidine ratios (1:1 – 1:5). These results support that the reactant and product of the redox couple process do not participate in adsorption-desorption activity at the surface of GCE electrode. (Fig. 14-17).

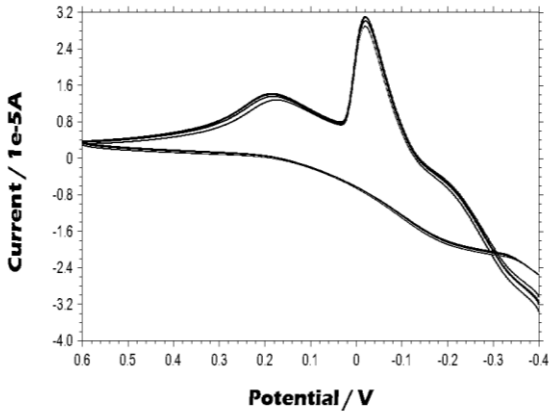


Fig. 15: Repetitive Cyclic Voltammograms at Glassy Carbon Electrode of Cu (II)-L-Histidine solution with 1:2 metal to ligand ratio at scan rate of 50mV/s in 0.1 M KCl as a supporting electrolyte; Temperature = 305±1K.

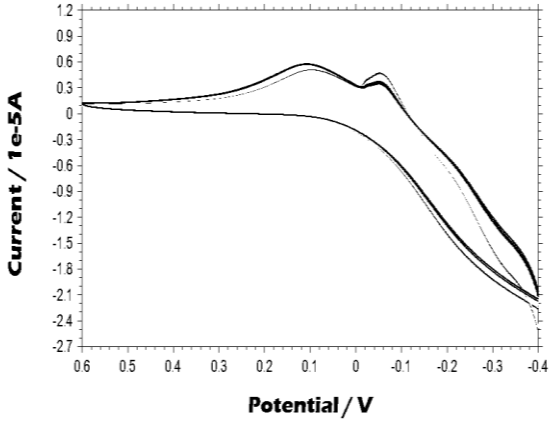


Fig. 16: Repetitive Cyclic Voltammograms at Glassy Carbon Electrode of Cu (II)-L-Histidine solution with 1:3 metal to ligand ratio at scan rate of 50mV/s in 0.1 M KCl as a supporting electrolyte at temperature = 305±1K.

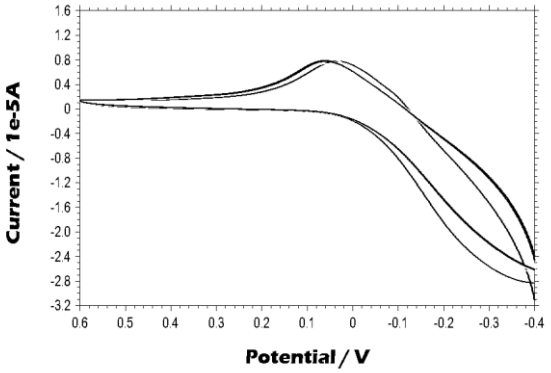


Fig. 17: Repetitive Cyclic Voltammograms at Glassy Carbon Electrode of Cu (II)-L-Histidine solution with 1:4 metal to ligand ratio at scan rate of 50mV/s in 0.1 M KCl as a supporting electrolyte at temperature = 305±1K.

Conclusions

It is concluded that Cyclic Voltammetry is powerful tool to study the behavior of metal ligand ratio to elucidate the structure. In this study Cu^{+2} solution is used as a reference and different metal to ligand ratio elucidated by Voltammogram. As a consequence, it is confirmed that metal–ligand 1:1 and 1:2 ratio gave better results than 1:3, 1:4 and 1:5 ratios. Furthermore, it is seen that no pre and post anodic or cathodic peak appeared during repetitive cycles of Voltammogram at Glassy Carbon Electrode in the presence of KCl (0.1 M) supporting electrolyte. It also confirmed that this is diffusion controlled process. Quantum mechanical calculations confirm stability of Cu^{+2}-L-Histidine (1:2) ratio complex by DFT method. It reflects that both experimental and computational results are consistent with Cu^{+2}-L-Histidine (1:2) ratio complex, both Voltammogram and optimization by DFT confirms stability of complex that exist as square planar geometry structure.

Conflict of Interests

Authors declare that there is no conflict of interest.

Acknowledgment

Authors would thanks to Chairperson of the Department of Chemistry Federal Urdu university of Arts Science and technology Gulshan-e-Iqbal Campus Karachi for providing the Instrumental facility of research work

References

1. S. Krupanidhi, A. Sreekumar, and C. B. Sanjeevi, Copper and biological health, *Indian J. Med. Res.*, **128**, 448. (2008).
2. N. Farrell, *Transition metal complexes as drugs and chemotherapeutic agents.* Kluwer Academic. Publisher, Dordrecht/ Boston. London., **11** (1989).
3. B.A. Chowdhury and R.K. Chandra, Biological and health implications of toxic heavy metal and essential trace element interactions, *Prog. food Nutr. Sci.*, **11**, 55. (1987).
4. A.A. Shaikh, J. Firdaws, Badrunnessa, S. Serajee, M. S. Rahman and P. K. Bakshi. Electrochemical studies of the pH dependence of Cu(II) reduction in aqueous Britton-Robinson buffer solution, *Int. J. Electrochem. Sci.*, **6,** 2333. (2011).
5. British Pharmacopoeia. *Published by The Stationery Office on behalf of the Medicines and Healthcare products Regulatory Agency (MHRA); **1,** 910-911*. (1999).
6. United State Pharmacopoeia. 24th Edition. United States Pharmacopeia Convention. Inc. Rockville, Md., 814 (2000).
7. V. B. Patel, K. N. Patel, M M. Shah and B. Ayank, Spectrophotometric determination of histidine hydrochloride monohydrate in pharmaceutical formulations, *Int. J. Pharm.Tech. Res*., **1,** 852. (2009).
8. D. Voet, and J.G. Voet "Biochemistry, 2nd ed. John Willey and Sons". New York (1995).
9. N.L. David, C. M. Micheal,. Lehninger's "Principles of Biochemistry, 4th Ed. WH Freeman and Co (2005).
10. The Merck Index. 14th Ed. White house Station NJ USA: Merck and Co. Inc.; Monograph Number: 0004720" (2006).
11. M. A. Motin, M. M. Rahman, M. Mia, K. S. Reza, A. M., Aziz, M. A. Hashem, Voltammetric study of Cu (II) in presence of aspartic acid and L-phenyl alanine at different pH media, *Anal. Bioanal. Electrochem.*, **7,** 264 (2015).
12. M.S. Rana, M. A. Rahman, and A.M.S. Alam, A Cyclic Voltammetric Studies of Complexation of Copper (II) with Thymine Using Glassy Carbon Electrode in Aqueous Medium, *Pak. J. Anal. and Environ. Chem.*, **15,** 13(2014).
13. H. Farhana, M. S. Rahman, E. Ahmed, P. K. Bakshi and A. A. Shaikh, A cyclic voltammetric study of the redox reaction of Cu (II) in presence of ascorbic acid in different pH media, *Dhaka Univ. J. Sci.*, **61**, 161(2013).
14. C.W.Yaw, W.T.Tan , W.S.Tan, C.H.Ng , W.B. Yap , N.H. Rahman , M. Zidan, Electrochemical Studies of Cu (phen) edda Interaction with DNA, *Int. J. Electrochem. Sci.*, **7,** 4692 (2012).
15. A. Habib, T. Shireen, A. Islam, N. Begum AND A.M. S. Alam, Cyclic voltammetric studies of copper and manganese in the presence of L-leucine using glassy carbon electrode, *Pak. J. Anal. and Environ. Chem.*, **7**, 96. (2006).
16. N. Nanda, M. Tanu, and S.M. Mayanna, Cyclic voltammetric study of biologically active metal ions with norfloxacin, *Indian J. chem. technol.*, **6,** 325. (1999).
17. K. D. Karlin, and J. K. Yandell, Redox behavior of blue copper model complexes. Redox potentials and electron-transfer kinetics of some copper (II)-copper (I) complexes with nitrogen and thio-ether donors. *Inorganic Chemistry.*, **23**, 1184. (1984).
18. I.M. Kolthof, and Y. Okinaka, Cyclic voltammetric studies of pH dependence of Cu (II) reduction, *J. Am. Chem. Soc.*, **81,** 2296. (1959).
19. M. S. Rana, M.A. Rahman, and A. M. S. Alam, A CV Study of Copper Complexation with Guanine Using Glassy Carbon Electrode in Aqueous Medium, *ISRN Electrochemistry.*, **1,** (2014).
20. B. Brever, F. Gutmann, and S. Hacobian, The polagrographic determination of antimony, *Aust. J. Sci. Res.*, **4,** 595. (1951).
21. B. Breyer, H. H. Bauer, and J. D. Beevers, Medical chemistry of cardiovascular agents and endocrines. *Aust. J. Chem.*, **14,** 479 (1961).
22. C. L. Aravinda, S.M. Mayanna, and V.S. Muralidharan, Electrochemical behaviour of alkaline copper complexes, *J. Chem. Sci.*, **112** , 543. (2000).
23. E. Ukpong and C. Obadimo, Mechanism and Cyclic Voltammetry of Cu (en) 2 $(ClO_4)_2$ in Aqueous 0.2 M $NaClO_4$, *Int. J. Electrochem. Sci.*, **9,** 4405. (2014).
24. F. M. Hawkridge, and H. H. Bauer, Kinetic and mechanistic study of the reduction of copper (II) in lithium nitrate using alternating current polarography, *Ana. Chem.*, **44,** 364. (1972).
25. G. Thomas, and P.S. Zacharias, Cyclic voltammetric studies of copper (II) amino acid complexes: electrochemical evidence for the generation of copper (I) complex as an intermediate, *Polyhedron.*, **4,** 811 (1985).
26. G. W. Tindall, and S. Bruckenstein, The simultaneous determination by stripping analysis of copper and silver in sulfuric acid supporting electrolyte using the platinum ring-disk electrode, *J. ElectroAnalytical Chem. and interfacial Electrochem.*, **22**, 367. (1969).

27. S. Chander, and D. W. Fuerstenau, The effect of potassium diethyldithiophosphate on the electrochemical properties of platinum, copper and copper sulfide in aqueous solutions, *J. ElectroAnalytical Chem. and interfacial Electrochem.,* **56,** 217. (1974).
28. Gaussian 09, Revision E.01, M. J.Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria,. M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. Sonnenberg, L. M. Hada, M Ehara,. K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y Honda, O. Kitao, H. Nakai, T.Vreven, J. A. Montgomery, Jr. Peralta, J. E. Ogliaro, F. Bearpark, M. Heyd, J. J. Brothers, E. Kudin, K. N. Staroverov, V. N. Kobayashi, R. Normand, J. Raghavachari, K. Rendell, A. Burant, J. C. Iyengar, S. S. Tomasi, J. Cossi, M. Rega, N. Millam, J. M. Klene, M. Knox, J. E. Cross, J. B. Bakken, V. Adamo, C. Jaramillo, J. Gomperts, R. Stratmann, R. E. Yazyev, O. Austin, A. J. Cammi, R. Pomelli, C. Ochterski, J. W. Martin, R. L. Morokuma, K. Zakrzewski, V. G. Voth, G. A. Salvador, P. Dannenberg, J. J. Dapprich, S. Daniels, A. D. Farkas, Ö. Foresman, J. B. Ortiz, J. V. Cioslowski, J. Fox, D. J. Gaussian, Inc., Wallingford CT,. 2009.
29. Gauss View , version 6.1, R. Dennington, T.A. Keith, and J.M. Millam, Semichem Inc., Shawnee mission, KS,. (2016).
30. T. F. Mastropietro , D. Armentano, E. Grisolia, C. Zanchini, F. Lloret, M. Julve, G. D-Munno Guanine-containing copper (II) complexes: synthesis, X-ray structures and magnetic properties, *Dalton Trans.,* **4**, 514 (2008).
31. E. Sletten, and B. Lie, Copper complex of guanosine-5'-monophosphate, *Acta. Cryst.,* **32,** 3301. (1976).
32. A. A. shaikh, Badrunnessa, J. Firdaws, M. S. Rahman, N. A. Pasha and P. K. Bakshi, A cyclic voltammetric study of the influence of supporting electrolytes on the redox behaviour of Cu (II) in aqueous medium, *J. Bangladesh Chem. Soc*., **24,** 158. (2011).