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Complexation of Iron by Dopamine Analogs; A Spectrophotometric and Potentiometric Study

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ABSTRACT

The chelation of Bio-essential metal, Iron, with dopamine analogs was studied at 30±2°C. Fe^{2+} formed intense color complex with these molecules with an absorbance maxima in visible region. A distinct peak of Fe-Carbidopa complex at 364nm with molar absorptivity of 1600 M^{-1} cm^{-1} was observed while that of Fe-Levodopa and Fe-Methyldopa were observed at 730nm with molar absorptivities of 306 M^{-1} cm^{-1} and 2300 M^{-1} cm^{-1}, respectively.

Potentiometric studies of the complex indicate that Fe(II) forms a 1:3 complex with levodopa and methyldopa while a 1:2 complex is found in case of carbidopa. The results obtained are consistent with the spectrophotometric studies.

Keywords: Iron, Dopamine analogs, stoichiometry, Molar absorptivity and Potentiometric analysis

1. INTRODUCTION

Carbidopa, Methyldopa and Levodopa are dopamine analogs present in antiparkinsonian drugs[1]. Dopamine plays very important role in function of central nervous, renal, hormonal and cardiovascular systems[2-3]. Its deficiency could result in several neurodisorders, the most common of which is Parkinsons[4].

Dopamine contains catecholic functional group due to which it is liable to interact with metals present in the physiological system[5-7]. Iron which has significant role in the biological system and is required for normal brain and nerve function through its involvement in cellular metabolism is assumed to bind through catecholic site of the molecules and therefore might lowers the efficiency of administered drug[8-9]. This interaction of Iron with Dopamine may also be evident by over accumulation of Iron in Parkinsonian brain[10]. In Pakinsonian brain there is an evidence of over loading of iron which might be the result of dopamine shortage in these patients. Role of iron in the pathogenesis of PD has been frequently reviewed[11-14]

Instead of direct Dopamine, Dopa of dihydroxyphenyl alanine (L-DOPA) is used as a precursor of dopamine that replaces missing dopamine through its conversion into dopamine in brain cells and therefore might reduce the symptoms of Parkinson's disease[15-16]. The treatment of this disease for most patients entails long term exposure to not only Levodopa (LD) but other dopamine analogs such as Carbidopa (CD) and Methyldopa (MD) are used along with to increase the efficacy of drug.

In the present study interaction of Dopamine and its analogs to Iron has been explored by potentiometric and spectrophotometric techniques.

2. MATERIAL AND METHODS

All chemicals used were of analytical grade supplied by Merck and Sigma while all the volumetric glassware used was of standard quality and special care was taken to wash them thoroughly before use. All the Stock solutions of desired molarities were prepared by dissolving calculated amount of solids in desired volume using deionized distilled water & 1% of 0.1M H_2SO_4 was added only in case of metal solutions. Fresh solutions were prepared each time.

Calculated amount of Metals and ligands were weighed using Metler Toledo B204-S balance such that final concentration of ligands were five times that of Metal and volumes were made up using distilled water which resulted into greenish colour complexes and variation in pH of each complex with each increment of 0.01M standard NaOH was measured using Precisa 900 pHmeter, Continuous stirring was carried throughout the experiment using JENEWAY1000 magnetic stirrer.

For spectral study 1.0mL of Fe(II) solution was added to 5.0mL of equimolar ligand solution. Solutions were allowed to stand for few minutes for completion of complex formation. Spectra were recorded in the region of 200nm-850nm using quartz cuvettes while Deionized distilled water was used as blank , on Schimadzu UV-1601 spectrophotometer and suitable wavelength was explored by comparing the spectra of each complex with metal and corresponding ligand.

In case of mole ratio determination, Different volumes of 0.005M ligand solutions were taken in 10.00 mL volumetric flasks with the help of pipette, then 1.0 mL of equimolar metal solution was added in each flask and capped with stopper, shook well, allowed to stand for 10 minutes & subjected to Genesys 6 Thermo Electron Corporation, to record absorbance at selected wavelength. The plot of absorbance vs ratio of ligand to metal concentration gave a curve. The straight line portions of obtained curves were extrapolated.

3. RESULTS AND DISCUSSION

The chelation of bio-essential metal, Iron with dopamine analogs was studied at 30±2°C temperature. Complexation of Carbidopa, Methyldopa and Levodopa was carried out with Fe (II). Each complex solution was scanned from 200nm-850nm to explore the absorbance maxima (Fig 1-3). For mole ratio determination equimolar metal and ligand

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solutions were prepared. Concentration of metal was kept constant. Different aliquots of ligand solution were added to metal and then absorbance was noted at their □max. The absorbance gradually increases with the rise of ligand to metal mole ratio (Fig 3). At high concentration of ligand the absorbance is independent of [L]. Tangent drawn on the curve in Fig 4-6 gave value of stoichimetric ratio in the complex. By this method mole ratio was found to be 1:2 for Fe(II)-CD while 1:3 in case of Fe(II)-MD and Fe(II)-LD complex respectively (Fig 4-6).

$$[Fe(H_2O)_6]^{2+} + H_2L \longrightarrow [Fe(H_2O)_4L] + 2H_3O^+ \quad \text{(1)}$$

$$[Fe(H_2O)_4L] + H_2L \longrightarrow [Fe(H_2O)_2(L)_2]^{2-} + 2H_3O^+ \quad \text{(2)}$$

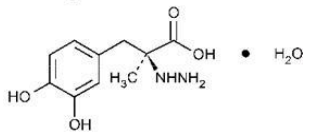
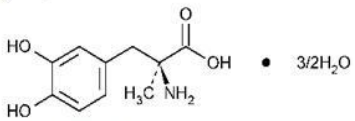
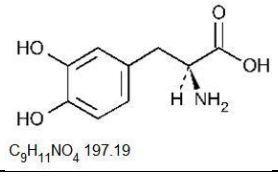
$$[Fe(H_2O)_2L_2]^{2-} + H_2L \longrightarrow [Fe(L)_3]^{4-} + 2H_3O^+ \quad \text{(3)}$$

Molar Absorptivity was calculated by dividing maximum absorbance of the complex to the metal concentration (Fig 4-6). The molar absorptivity was found highest for Fe-MD= 2300 M^{-1} cm^{-1} while 1600 M^{-1} cm^{-1} for Fe-CD and very low for Fe-LD complex (Table 1).

The pH of complex and ligand solutions was recorded after addition of each aliquot of standard NaOH. The difference in pH of the complex and ligand is a clear evidence of complexation of Fe^{+2} with Carbidopa, Methyldopa and Levodopa. This study also revealed that all the three ligands has capability to release $3H^+$, out of which two are released in a very close range of pH confirming their presence in a very similar environment. This indicates that both the OH of catecholic groups release their H^+ simultaneously and latter –COOH group releases H^+ (Fig 7-9).

It was also observed in titration of Carbidopa, Methyldopa and Levodopa complexes of Fe^{+2} that there is a very short difference of pH in maintenance of M- ML_1 and ML_1-ML_2 equilibria while ML_2- ML_3 equilibria are achieved at higher pH (Fig 7-9).

Table-1: Spectral Properties of Fe-dopamine Complexes

Structure of Ligand	Complex	Selected Wavelength (nm)	€ $M^{-1}cm^{-1}$	pH	Stoichio-metry
Carbidopa  $C_{10}H_{14}N_2O_4 \cdot H_2O$ 244.24	Fe-$(CD)_n$	364	1600	4.4-4.9	1:2
Methyldopa  $C_{10}H_{13}NO_4 \cdot 1½H_2O$ 238.24	Fe-$(MD)_n$	730	2300	4.2-4.5	1:3
Levodopa  $C_9H_{11}NO_4$ 197.19	Fe-$(LD)_n$	730	302	4.2-4.4	1:3

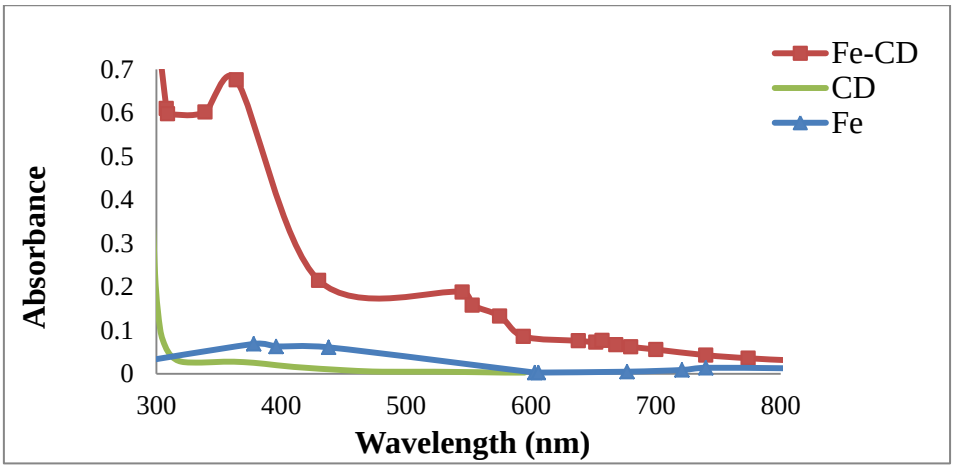


Fig-1: Spectra of Fe-Carbidopa complex (1:5mL equimolar Fe(II)) & CD in 1% 0.1M H_2SO_4 at Temperature=30±2 °C, CD and Fe(II) solutions.

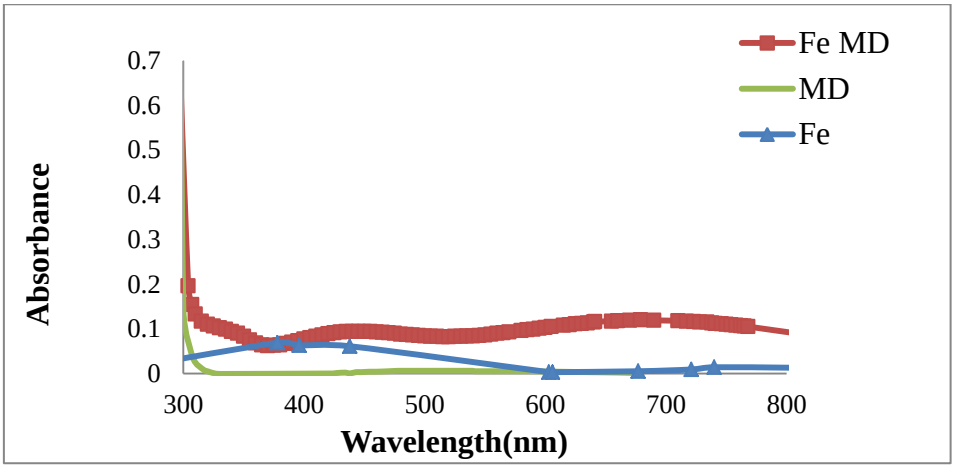


Fig-2: Spectra of Fe-Methyldopa complex(1:5mL equimolar Fe(II)) & MD in 1% 0.1M H_2SO_4 at Temperature=30±2 °C, MD and Fe(II) solutions.

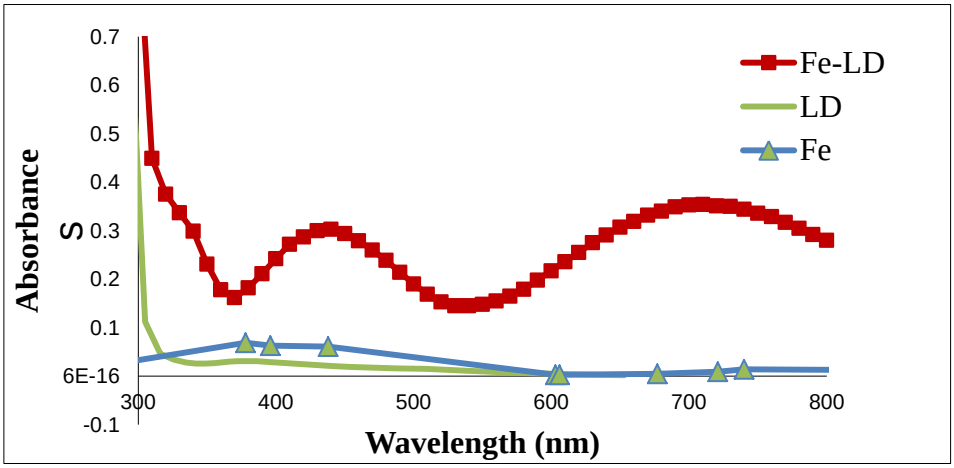


Fig-3: Spectra of Fe-Levodopa complex(1:5mL equimolar Fe(II)) & LD in 1% 0.1M H_2SO_4 at Temperature=30±2 °C, LD and Fe(II) solutions.

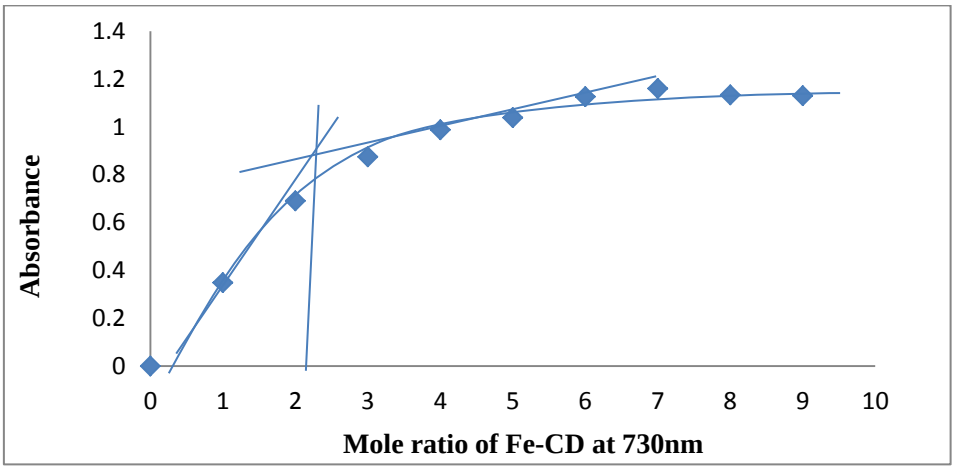


Fig-4: Plot of Moleratio of Fe-CD(0.05mM), at Temperature=30±2°C

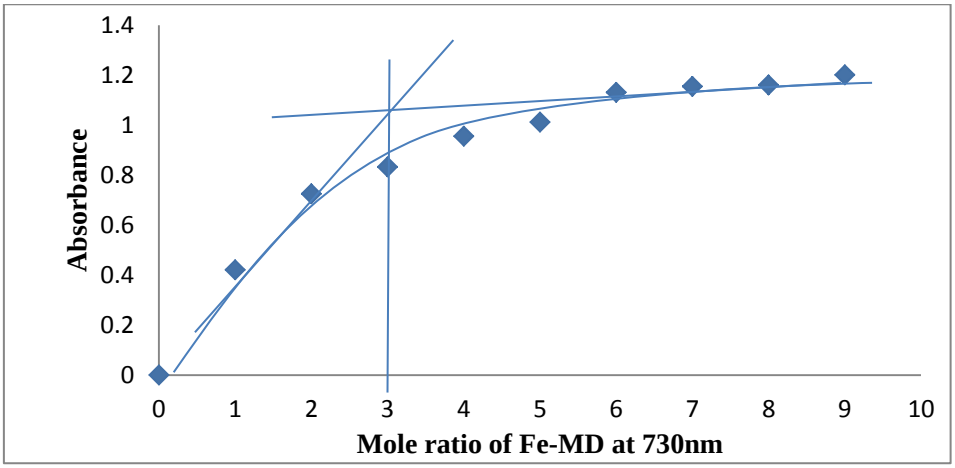


Fig-5: Plot of Moleratio of Fe-MD (0.05mM), at Temperature=30±2°C

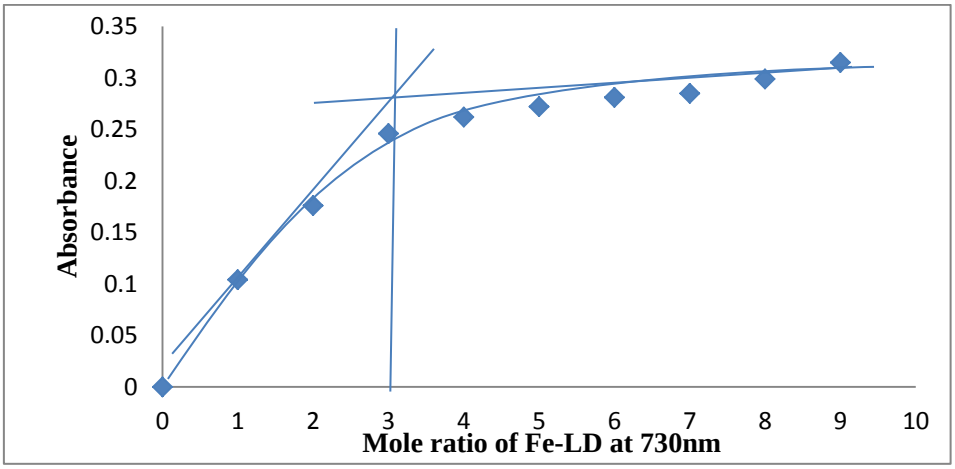


Fig-6: Plot of Moleratio of Fe-LD (0.05mM), at Temperature=30±2°C

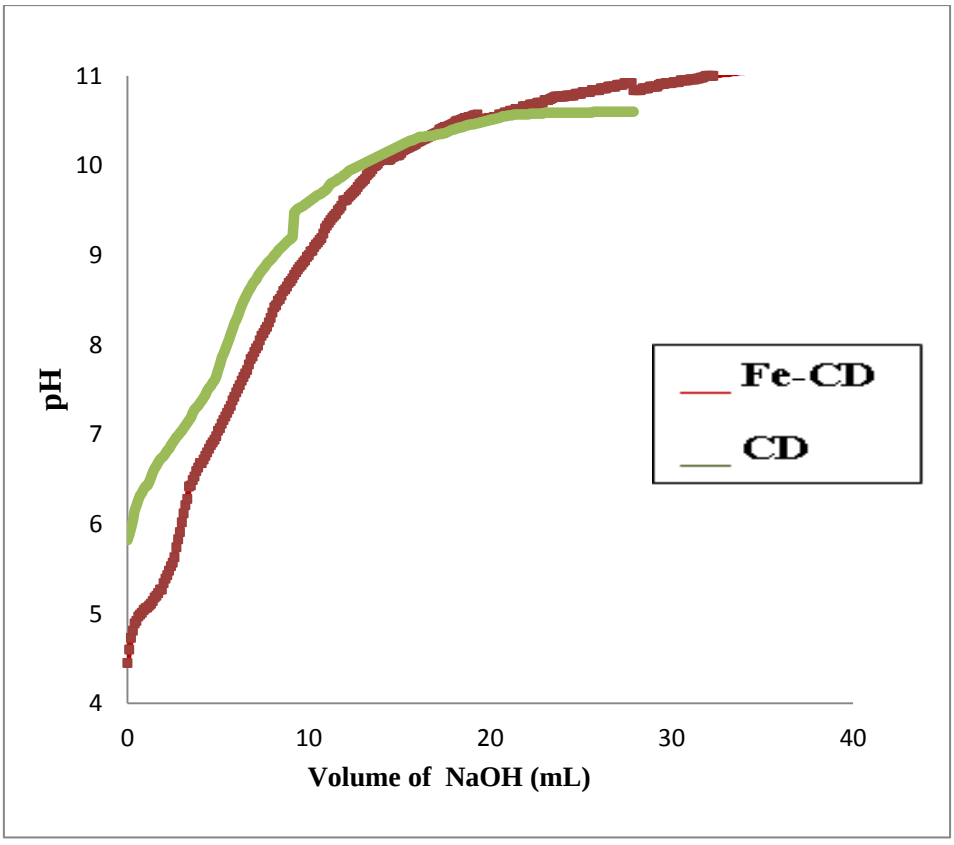


Fig-7: Potentiometric titration of Fe-CD & CD. Fe(II) = 0.05mM, CD = 0.25mM, NaOH = 0.01M and Temperature=30±2°C

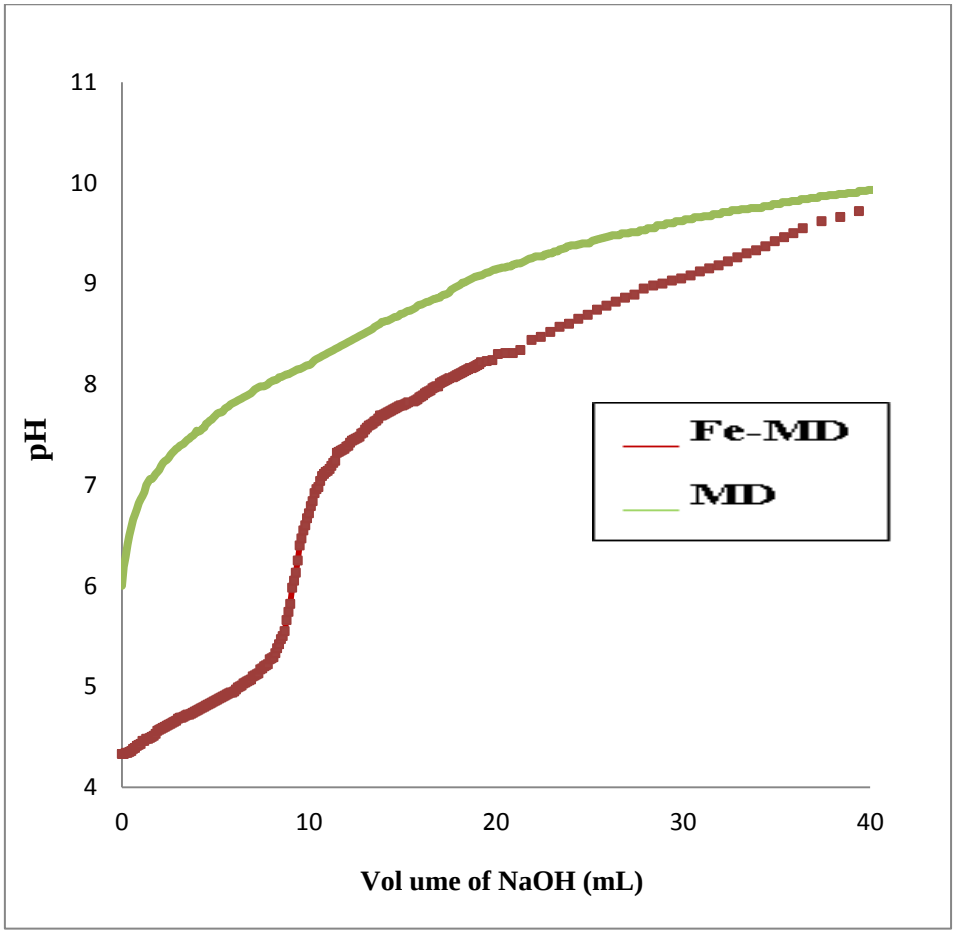


Fig-8: Potentiometric titration of Fe-MD & MD. Fe(II) = 0.05mM, MD = 0.25mM, NaOH = 0.01M and Temperature=30±2°C

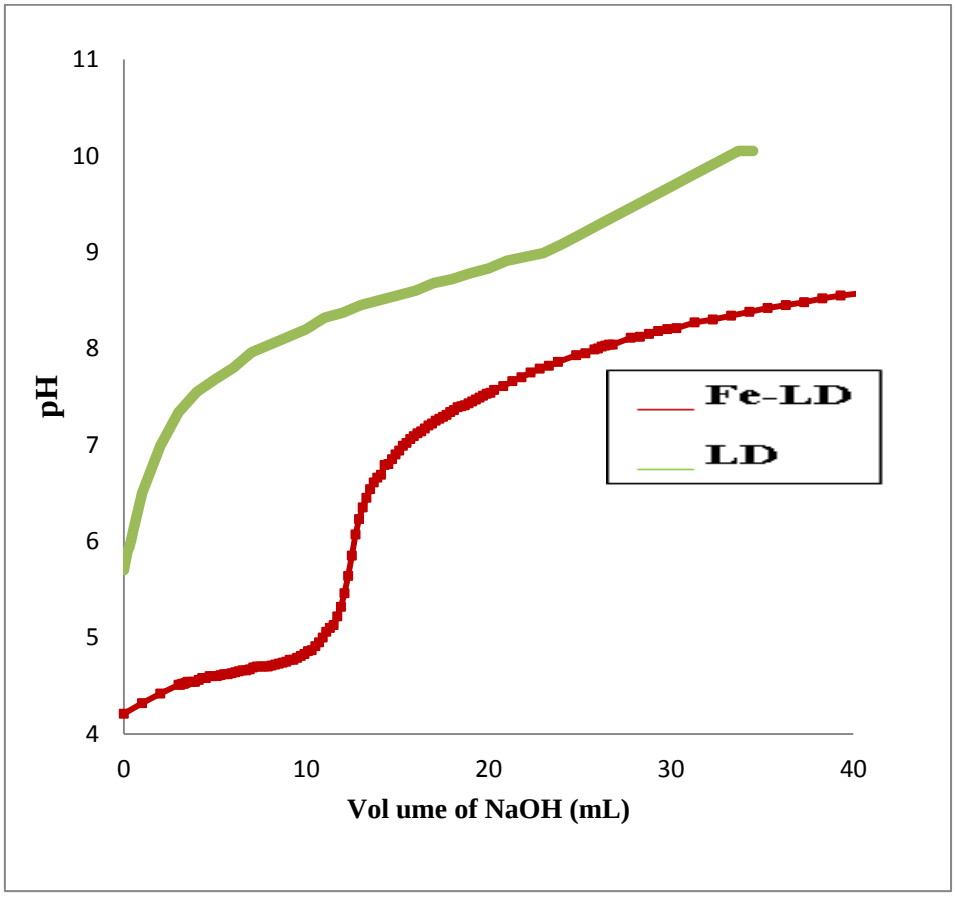


Fig-9: Potentiometric titration of Fe-LD & LD. Fe(II) = 0.05mM, LD = 0.25mM, NaOH = 0.01M and Temperature=30±2°C

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