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RESEARCH ARTICLE

Interaction of Antiparkinsonian Drug molecule, (-)-3-(3,4-dihydroxyphenyl)-L-alanine with Bioessential Metals Study by Simple Spectrophotometric Method

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Abstract

Due to significance of metals and their high affinity towards oxygen and nitrogen donor ligands, present in the biological system, the interaction of (-)-3-(3,4-dihydroxyphenyl)-L-alanine with few bioessential metals was selected to study, using spectrophotometry. Metal and ligand were mixed in 1:5 ratio of metal and ligand. The complex solutions were then scanned from 300 to 800 nm. Spectra of Cr^{III}, Mn^{VII}, Mn^{IV}, V^{V}, V^{III}, Fe^{III} and Fe^{II} complexes were recorded on Shimadzu spectrophotometer model UV-160A. λ_{max} of mentioned metal complexes were found to be as 410 & 590 nm for Cr^{III}, 303 & 477 nm for Mn^{VII}, 478 nm for Mn^{IV}, 510 nm for V^{V} and 460 nm for V^{III}. While, that of 430 & 730 nm for both Fe^{III} and Fe^{II}.

In Addition to that the stoichiometry of Mn^{VII}, Mn^{IV}, Fe^{III}, Fe^{II} with LD was evaluated by mole ratio method, providing consistent results. Using stoichiometric data, overall formation constant, log K_f, were evaluated for all complexes. It was found 12.45 for Mn^{VII}-LD, 9.64 for Mn^{IV}-LD, 9.75 for Fe^{III}-LD and 11.45 for Fe^{II}-LD complexes.

INTRODUCTION

The bio-essential metals are organized in two groups, Na, K, Mg and Ca are under the heading of macro nutrient, while V, Cr, Mn, Fe, Co, Ni, Cu and Zn are classified as micro nutrients [1-2]. The most important factor of these minerals is bioavailability, which depends on food sources that can restrain absorption in the body [3]. The source of metals is not only the food but the drugs, used to cure several diseases [4].

Every metal have its biological properties as Chromium is a cofactor that takes part in maintaining the body sugar levels [5]. Its insufficiency may provoke glucosuria and hyperglycemia. Often in combination with Fe, and in many minerals, Mn is found as a free element in nature [6]. Patients with severe hepatitis and posthepatic cirrhosis, in dialysis patients and in patients suffering heart attacks are affected with significant rise in Mn concentrations [7-12]. Ferrous ion (Fe^{II}), is an essential trace element necessary for almost all living beings [13]. Ferritin, the iron storage protein, is synthesized by ferritin molecules and PC12 cells, which are known to be present in axons of neuronal cells [14-16]. Iron storage could contribute by both the ferritin and dopamine systems, in dopaminergic cells. Additionally, it can be considered that Fe-dopamine structures in neuritis outgrowths might also be related to the axonal transportation of Fe to the synapse from the cytosol [17-18]. It is unlikely that a person would take too much Fe [19]. However, in children, sometimes Fe poisoning may develop by swallowing high quantity of Fe supplements. Symptoms of Fe poisoning include **Parkinson's disease** (PD) [20-23].

Parkinson's disease is a chronic disease, upshots from annihilation of the substantia nigra due to which a progressive disarray of the central nervous system with the consequence of deterioration of those neurons that usually bring forth the neurotransmitter dopamine. Basically dopaminergic neurons mostly die-off in PD patients [24-27].

Derivative of Dopamine Precursor, Levodopa (LD) is (-)-L-amino-(3,4-dihydroxybenzene) propanoic acid [28] or **(-)-3-(3,4-dihydroxyphenyl)-L-alanine** (Figure 1), which is Amino acid derivative of catechol. According to stereoisomerism it is levorotatory stereoisomer of dopa [29]. Its d-enantiomer leads to clinical side effects [30].

Keeping in view the role of metals in PD, the present work was planned to evaluate the interaction of LD with those metals which are reported to have some involvement in normal brain function. Therefore spectral study of Cr, V, Mn and Fe was carried. While, stoichimetry and overall formation constants of Mn and Fe is investigated.

EXPERIMENTAL

Analytical grade reagents were used in the experiments. Metal salts ($Cr(NO_3)$, $KMnO_4$, MnO_2, V_2O_5, V_2O_3, $FeCl_3.6H_2O$ and $Fe(NH_4)_2(SO_4)_2.6H_2O$ were of Merck and Levodopa was obtained from Wild Wind. Stock and sample solutions were prepared in CO_2 free distilled deionized water.

Absorbance Maxima

Absorbance maxima of each metal complex i.e. Cr^{III}, Mn^{VII}, Mn^{IV}, V^{V}, V^{III}, Fe^{III} and Fe^{II}, was explored by mixing aliquots of metal ion solution to enough excess of ligand solution. Within a few seconds color was developed. Following that, the each complex solution was subjected to scanning in UV-visible region, on double beam Spectrophotometer, Shimadzu UV-160A and that λ_{max} were established (table 1).

Mole ratio

Experiment was carried out in triplicate, having an accurate amount of the metal salts and the ligand was taken to prepare respective solutions in deionized distilled water. Calculated, aliquots of ligand solution were added in 5.0×10^{-4} M metal solution and volume was kept constant for all. Flasks were capped with stopper, shook well & subjected to Genesys 6 Thermo Electron Conforation for the recording of absorbance of the metal complexes at selected λ_{max}, from the recorded spectra. Throughout the experiment the temperature was maintained at 25 ± 1ºC [31].

RESULTS

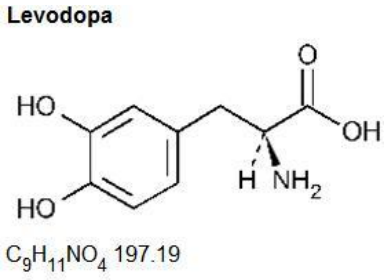

Figure 1. (-)-3-(3,4-dihydroxyphenyl)-L-alanine Commonly known as Levodopa

Spectral Characteristics

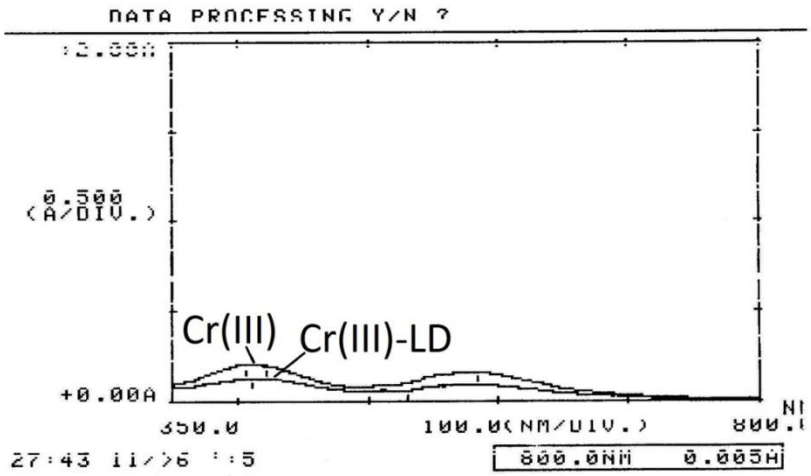

Figure 2. Overlay Spectra of Cr^{III}-LD Complex

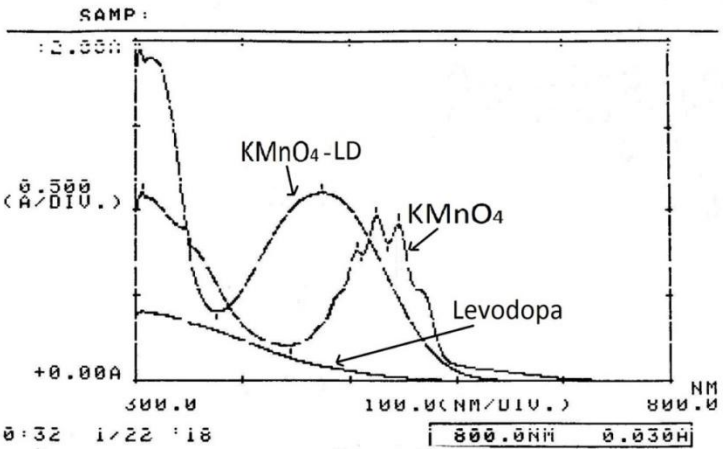

Figure 3. Overlay Spectra of Mn^{VII}-LD Complex

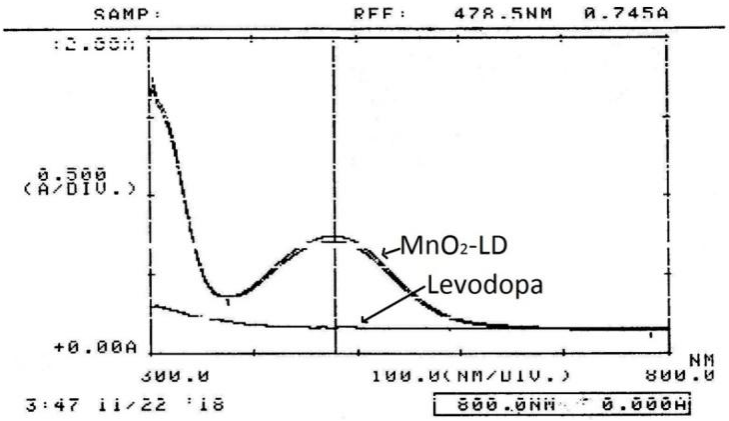

Figure 4. Overlay Spectra of Mn^{IV}-LD Complex

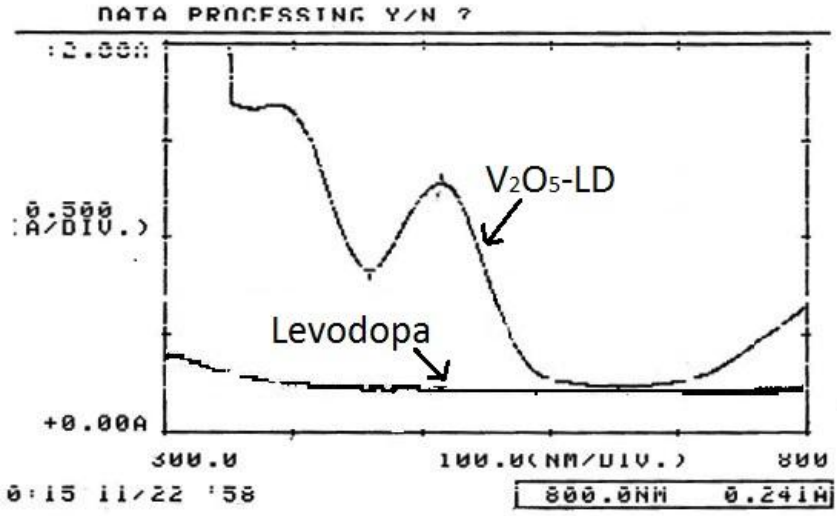

Figure 5. Overlay Spectra of V^{V}-LD Complex

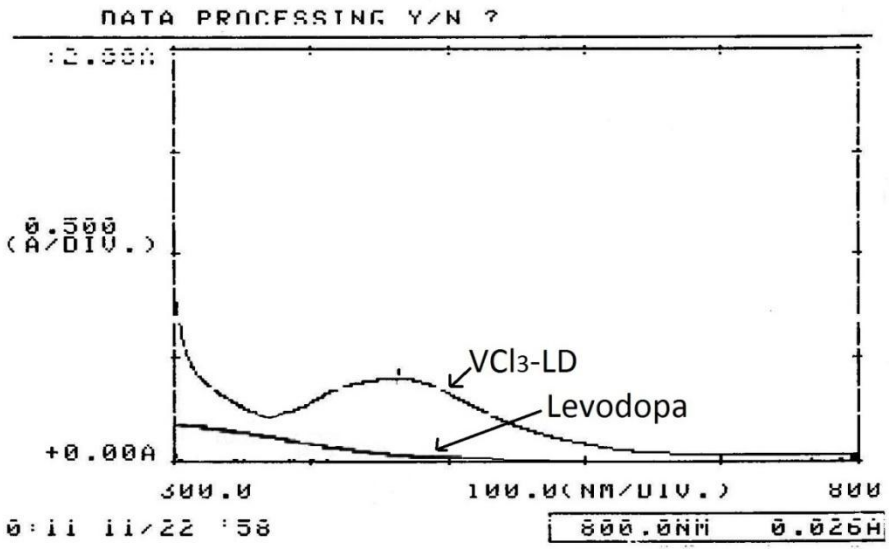

Figure 6. Overlay Spectra of V^{III}-LD Complex

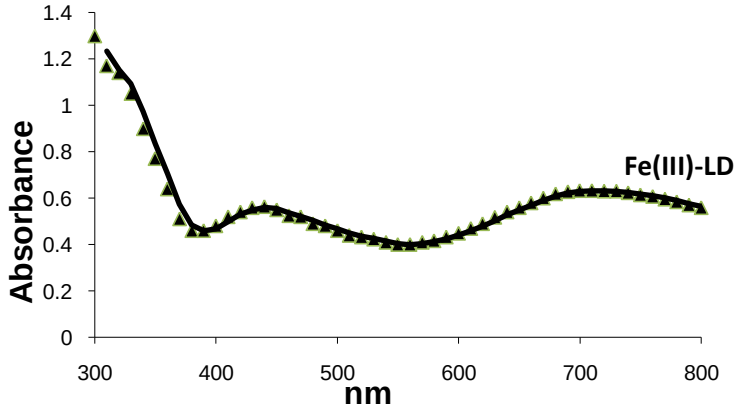

Figure 7. Spectra of Fe^{III}-LD complex

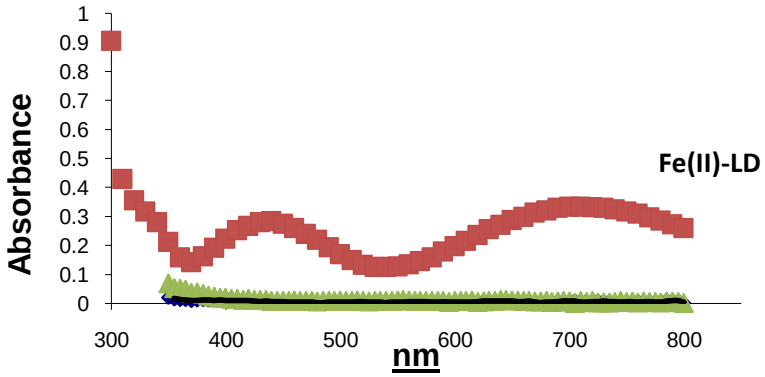

Figure 8. Spectra of Fe^{II}-LD Complex

Stoichiometry

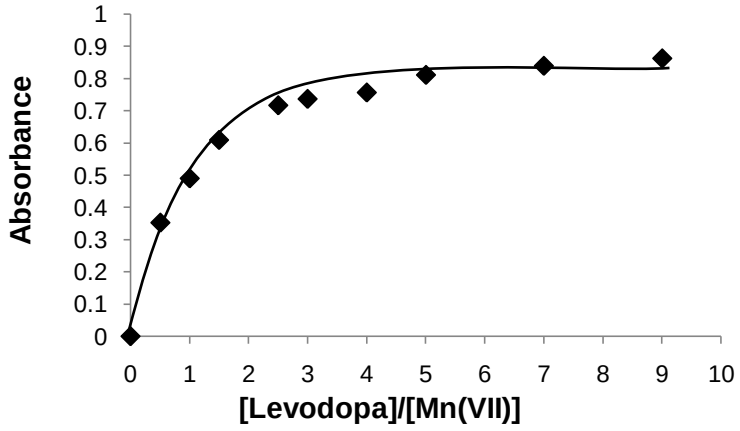

Figure 9. Mole Ratio Graph of Mn^{VII}-LD Complex, Temp. = 25±1°C, $[Mn^{VII}] = 5.0 \times 10^{-4}$ M, $\lambda_{max} = 477$nm

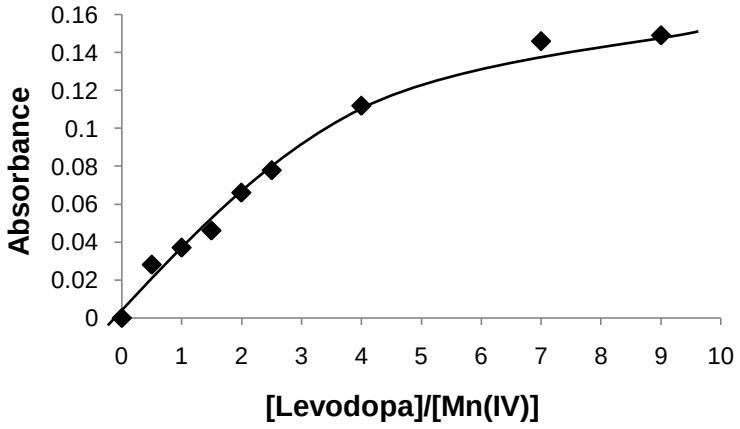

Figure 10. Mole Ratio Graph of Mn^{IV}-LD Complex, Temp. = 25±1°C, $[Mn^{IV}] = 5.0 \times 10^{-4}$ M, $\lambda_{max} = 478$ nm

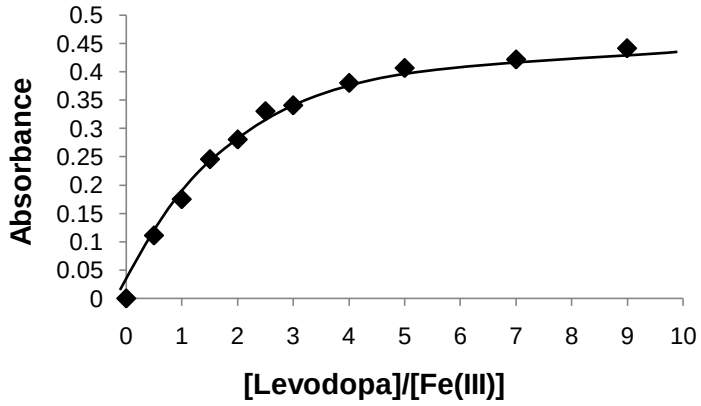

Figure 11. Mole Ratio Graph of Fe^{III}-LD Complex, Temp. = 25±1°C, $[Fe^{III}] = 5.0 \times 10^{-4}$ M, $\lambda_{max} = 730$ nm

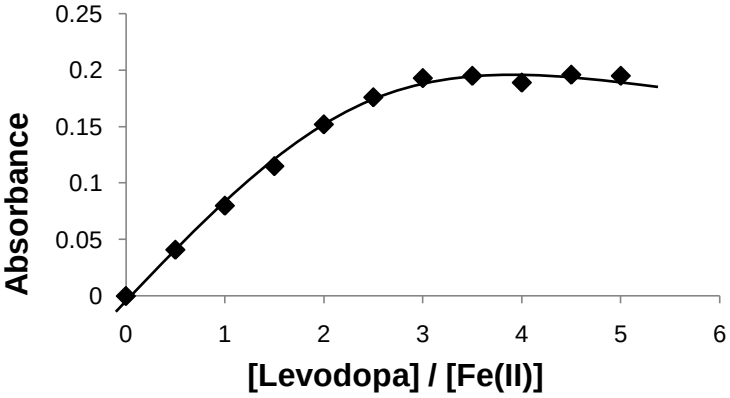

Figure 12. Mole Ratio Plot of Fe^{II}-LD Complex, Temp. = 25±1°C, $[Fe^{II}] = 5.0 \times 10^{-4}$ M,

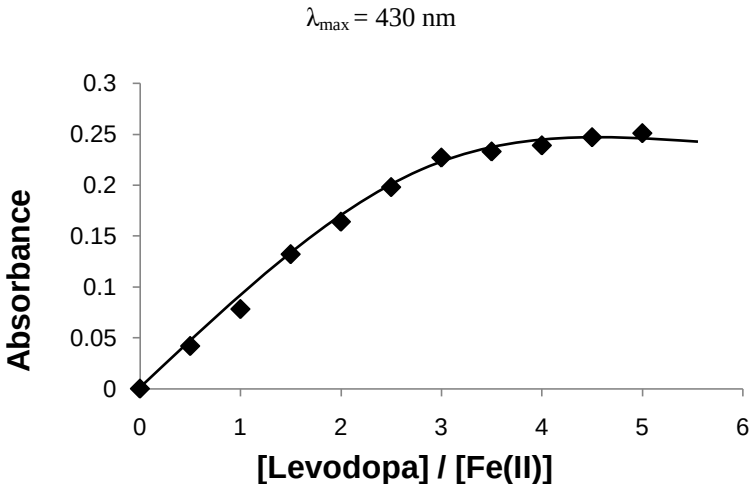

Figure 13. Mole Ratio Plot of Fe^{II} -LD Complex, Temp. = 25±1°C, $[Fe^{II}] = 5.0 \times 10^{-4}$ M, λ_{max} = 730 nm

Table 1. Significant Peaks of LD complex with different metals in non buffered Medium

Metals Complexed with LD	Peaks (nm)	Absorbance	Peaks (nm)	Absorbance
Cr^{III}	410	0.015	590	0.015
Mn^{VII}	303	1.938	477	1.105
Mn^{IV}	478	0.745	------	------
V^{V}	510	1.340	------	------
V^{III}	460	0.480	------	------
Fe^{III}	430	0.473	730	0.630
Fe^{II}	430	0.710	730	0.780

Table 2. Formation Constants Evaluated from Mole Ratio Method

Metals-LD	λ_{max} (nm)	Log K_f values	Stoichiometry
Mn^{VII}	477	12.45	1:3
Mn^{IV}	478	9.64	1:3
Fe^{III}	730	9.75	1:3
Fe^{II}	730	11.45	1:3

DISCUSSION

Each metal ion solution was mixed with LD solution in a molar ratio of 1:5 and the resulting spectrum of solution was recorded on Shimadzu model number UV-160A, in the range of 200 nm to 800 nm. Ligand and metal solutions were also scanned under the same conditions. For comparison, the spectra of metal, LD and metal-LD complex were combined in the same figure (Fig2-8). LD was allowed to react with many bio-essential metals including Cr^{III}, Mn^{VII}, Mn^{IV}, V^{V}, V^{III}, Fe^{II} and Fe^{III}.

Cr^{III}- LD Complex

Combined spectra of the Cr^{III} complex was given in Figure 2, having two peaks at about 410 nm and 590 nm. The peak of complex is not clearly distinguishable from the metal spectra. The overlay scan also has two peaks at about 410 nm and 590 nm as in the spectra of metal while the absorbance is low due to the effect of dilution.

Mn^{VII}- LD Complex

The λ_{max} of Mn^{VII}-LD complex was clearly distinguished from the Mn^{VII} and LD spectrum. Overlay spectra (Figure 3) clearly showed complex formation due to significant absorbance. The two peaks at 477 nm and 303 nm were obtained (Table 1). However the metal spectra showed significant absorbance at 545 nm, 525 nm, 507 nm and 307 nm. Here it is clear that the peak at 303 nm is same, present in the metal ion spectrum, whereas the other peaks of metal, in the range of 545.0 nm to 507.0 nm were shifted to 477.0 nm giving a single peak (Figure 3). It is a clear evidence of complexation.

Mn^{IV}- LD Complex

The complex of Mn^{IV} with LD showed a distinct peak at about 478 nm. On camparision with metal and LD spectra a clear change in Mn^{IV}-LD solution is an evidence of complexation (Figure 4).

V^{V} - LD Complex

V^{V}-LD complex showed the maximum absorbance at 510 nm, which was not found in LD and metal spectra. This observation verifies the chelation of V^{V} by LD (Figure 5).

V^{III}- LD Complex

V^{III}-LD has a significant peak at 460 nm, evidence of complexation (Figure 6).

Fe^{III}- LD Complex

Spectral presentation of the complex of Fe^{III} with LD was given in Figure 7, showing prominent peaks at 425 nm and 736 nm. The peak of complex is distinguishable from the Ligand spectra. LD spectra do not show any peak in this region.

Fe^{II}- LD Complex in Aqueous (non-buffered) Medium

Figure 8 showed Fe^{II}–LD complex spectra, taken from 300 nm to 800 nm, which shows λ_{max} at 430 nm and 730 nm.

Mole Ratio Spectra of Mn^{VII}, Mn^{IV}, Fe^{III} and Fe^{II} With LD

The graphical representation of the absorbances against the mole ratio of studied metals-LD complexes at their respective λ_{max} (Table 1) is given in Figures 9 to 13. Mole ratio, of 1:3, in each case of Mn^{VII}, Mn^{IV} and Fe^{II} complexes, with LD was evaluated (Figure 9 to 13). Similarly in the complex of Fe^{III}-LD, 1:3 M to L ratio was found, the reactivity of Fe^{III} is higher than the other metals.

CONCLUSION

Spectral Studies were carried with many metals such as, Mn^{IV}, Mn^{VII}, V^{III}, V^{V}, Cr^{III}, Cu^{II}, Fe^{II} and Fe^{III} in distilled deionized water. All the complex solutions showed charge transfer bands except the Cr^{III}. V^{III} shows maximum absorbance at 460 nm while V^{V} at 510 nm. Mn^{IV} and Mn^{VII} showed identical λ_{max} at 478 nm. Similarly in case of

iron-LD complex, λ_{max} is found identical regardless of starting oxidation state of metal, evidence of same complex in both the cases.

Complexes of LD and iron showed two peaks which is characteristics of d^5 system, therefore the spectra of complex evidenced the presence of iron in +3 form.

Overall Formation Constant, the log K_f, was found high in all cases. Fe^{II}-LD complex has maximum log K_f value ≈ 12, regardless of wavelength (selected). These values were also determined by Job's plot method, for Fe^{II}-LD complex only [32]. The result is close to the values obtained by mole ratio method (Table 2). Mn^{VII}-LD showed much higher log K_f value closer to Mn-EDTA i.e. 13.56 [33], while Fe^{III} and Fe^{II}-LD complexes have also high K_f values as reported for these metal with various ligands [33].

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