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Potentiometric Studies on Stability Constant of the Complexes of Some Essential Transition Metal Ions with *L-Valine*

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Abstract The interaction of Co (II), Ni (II) and Cu (II) metal ions and the biologically important amino acid *L-Valine,* (2-amino-3-methyl butanoic acid) have been investigated. The potentiometric technique was used to study these intraction at 313.15 ± 0.1 K in the absence and in the presence of ionic strength of 0.1 M (NaCl) in aqueous medium. The data obtained under the above experimental conditions were used to evaluate the values of proton-ligand and metal-ligand stability constants using Irving-Rossotti titration technique. The formation of the 1:2, (M:L), binary complexes are confirmed by the corresponding pH titration curves. The values of logK and logβ were calculated and found in the order of copper (II) > nickel (II) > cobalt (II).

Keywords: Metal ions, Metal complexes, *L-Valine*, Potentiometric method, Stability constant.

تحضير ودراسة طيفية وحرارية لمعقدي النيكل (II) والبلاديوم (II) مع مرتبط ثلاثي التسنن وفعاليتها في انقسام DNA

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الملخص تم دراسة تفاعل أيونات Co^{2+} (II) و Ni^{2+} (II) و Cu^{2+} (II) والحمض الأميني الفالين عن طريق تقنية المعايرات الجهدية عند 313.15 ± 0.1 كلفن في غياب وجود قوة أيونية 0.1M من كلوريد الصوديوم (NaCl) في وسط مائي . تم استخدام البيانات التي تم الحصول عليها في ظل الظروف التجريبية المذكورة أعلاه لتقييم قيم ثوابت الاستقرار للحمض الاميني الفالين و ايضا ثوابت الاستقرار للمعقدات الناتجة من تفاعله مع ايونات المعادن Co^{2+} (II) و Ni^{2+} (II) و Cu^{2+} (II) وذلك باستخدام تقنية معايرة Irving-Rossotti. استخدمت المعايرات الجهدية لحساب نسبة المرتبط الى ايون المعدن فوجدت (L:M) 2:1. تم حساب قيم log K و log β ووجدت لتتبع الترتيب التالي معقد النحاس (II)> معقد النيكل (II)> معقد الكوبالت (II).

الكلمات المفتاحية: أيونات المعادن، معقدات المعادن، الحمض الاميني الفالين، الطريقة الجهدية، ثابت الاستقرار.

Introduction

Today, the study of metal complexes of biological active ligands is an important purpose, because the study of these complexes will be helpful to understand the interaction between the protein and metals in the biological systems. In addition, the stability and thermal values of these complexes will help us to identify the atoms or groups that are responsible for binding to metal ions used in retention of toxic heavy metal ions [1, 2].

Cupper among essential transition metal is important for many enzymes, particularly those catalyzing physiologically important reactions. Cu (II) has a strong ability to form complexes with proteins, peptides, enzymes in the living organisms [3, 4]. Examples of copper-containing compounds are tyrosinase and ferroxidase and Hemocyanin [3]. Cobalt is used by animals in form of B_{12} and B_9 vitamins that play the vital role in the natural production of red blood cells in animals. Moreover, Nickel is important because of its ability to replace other metal ions in enzymes and proteins, to bind to cellular compounds containing O^-, S^- and N^- atoms such as enzyme and nucleic acids. Ni(II) is essential for the healthy life of humans and animals and its deprivation profoundly impairs intestinal absorption of iron and thus causes anemia. Both glucose and glycogen concentrations in the liver and serum are reduced by 90% on nickel depletion[5].

Among the variety bioactive ligands, the amino acids have special importance compared to other chemical compounds in the sense that they are regarded as the foundation stones of living organisms. Thus, studying their chemical properties becomes very necessary to explain their behavior and its potential applications. Among these properties are stability constants and thermodynamic of complexes they form with various metal [6, 7].

L-Valine is an α-aminoacid that is used in the biosynthesis of proteins [8], where it is an essential amino acid in humans, meaning the body cannot synthesize it; it must be obtained from the diet, which sources are foods. L-Valine (Fig.1) plays an important role in muscle synthesis and maintenance, stress management. In addition, it is important for children growth and the functioning of the nervous system. Early studies show that this role may help *L*-Valine to manage nervousness and insomnia because it has a role in forming the myelin sheaths that cover nerve cells. Valine, like other branched-chain amino acids, is associated with insulin resistance: higher levels of Valine are observed in the blood of diabetic humans [8, 9].

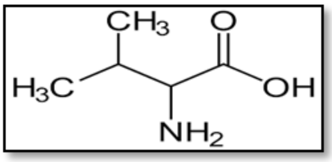


Fig. 1: Chemical structure of L-Valine (2-amino-3-methyl butanoic acid)

Amino acids can act as coordinating agents through their amino groups (NH_2) and carboxylic (COO^-). These groups provide a more diverse coordination activity towards heavy metal ions. Thus, it can be used to isolate heavy metal ions and obtain safer drugs or antidote to metal poisoning. Leach[10] reported an amino acid derivative whose copper(II) complexes exhibited a general preference for L-amino acids. A set of potentiometrically determined stability constants indicated that copper (II) complexes of N-carboxy methyl-L-Valine, [Cu (N-Cm-L-Val)], formed stronger complexes with L-leucine, L-phenylalanine, L-alanine, L-serine, and D-Valine than with the respective antipodes[11]. Previously, there had been no reports of a ligand exhibiting such a general stereoselectivity, although it appears now that N-benzyl-L-proline has a similar characteristic [12]. Thus it was decided to pursue the chemistry of this particular L-Valine compound and its analogs. Antonili et al [13] studied the silver complexes of some N-protected amino acids such as N-acetyl and benzoyl–glycine, alanine, Valine, leucine and tryptophan.

Singh and et al. [14] studied about the interaction of metal ions (Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+}) with N-benzoyl-L-Valine, N–benzoyl, glycol-L-Valine and isovaleric acid. They also used the pH titration technique to evaluate stability constants at 25 ^0C, 35 ^0C and 45 ^0C at 0.15 M KNO_3 ionic strength in 50 volume % water-dioxane medium. Only 1:1 metal complexes were formed with stabilities.

The present paper deals with the determination of protonation constants of *L*-Valine and the stability constants of the complexes formed by Co(II), Ni(II) and Cu(II) with L-Valine using potentiometric pH method at (313.15±0.1 K) temperature and in the absence and in the presence anionic strength 0.1 mol L^{-1} (NaCl).The method of Calvin-Bjerrum [15, 16] as adopted by Irving and Rossotti [17, 18] has been employed to determine log K values.

2. Experimental

2.1. Materials

All chemicals utilized in this investigation were of the analytical reagent grade (AR) quality and of the highest purity. L-Valine (Fluka, >99%), metal salts including $CuCl_2.2H_2O$ (T-Baker lab chemicals, ≥ 99.99 %), $CoCl_2.6H_2O$ (Surechem Products, 98.8 %), $NiCl_2.6H_2O$ (Surechem Products, 98%), Sodium Hydroxide (Shandong, 98.8%) and Hydrochloride acid (Scharlau-chemise, 36%) and Sodium Chloride (BDH Chemicals).

2.2.Solutions: Hydrochloric acid stock solution was prepared and titrated against standardized sodium hydroxide. The stock solution of *L*-Valine (0.004M) was freshly prepared before use by dissolving accurately (0.04686g) solve with a minimum quantity of distilled deionized water. Carbonate-free sodium hydroxide solution was prepared and standardized against standard oxalic acid solution before starting an experiment. The stock solution of each metal salts was prepared by dissolving the required quantities (0.47586g Co(II), 0.47542g Ni(II), and 0.34096g Cu(II)) in deionized water. The stock solution of metals salt was standardized by EDTA titrations.

2.3. Apparatus

Potentiometric titration performed by using pH-meter model (Thermoelectric Corporation/ Orion3 Star (pH Benchtop) (accuracy ±0.002) with a glass and calomel electrodes assembly. The pH-meter was standardized before each titration with a buffer solution of pH = 4.01, 7.00 and 10. The temperature was maintained constant (± 0.1) by a Grant Instruments (Cambridge) Ltd/SUB28 Thermostat Water Bath Apparatus.

2.4. Procedure

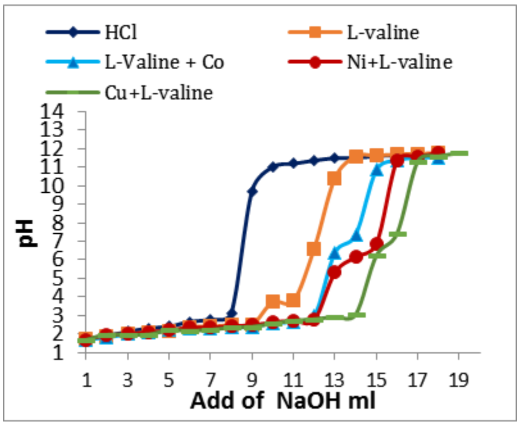
The experimental procedure involved the potentiometric titration of the following sets of solutions:

1) Acid titration: HCl (0.1M, 10 ml)
2) Ligand titration: HCl (0.1M, 10 ml) + *L*-Valine (0.004 M, 10 ml).
3) Metal + ligand titration: HCl (0.1M, 10 ml) + L-Valine (0.004 M, 10 ml) + metal ion (0.004M, 10 ml).

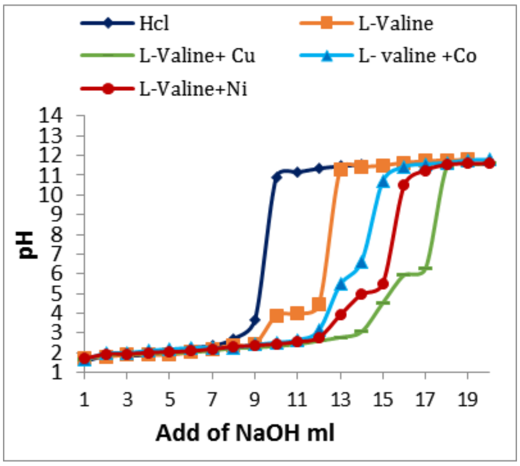
The total volume used in each cell was 50 ml and in the absence and in the ionic strength 0.10 M (NaCl) and at two temperatures 313.15±0.1 K in all sets. The titrations performed with carbonate-free standardized 0.10 M NaOH solution. The three curves were obtained from the plots of pH versus volume if alkali required and are referred to as (i) acid (ii) ligand (iii) complex titration curves (Fig. 2).

3. Result and Discussion

The proton dissociation constants of the amino acid, L-Valine, and its complexes of Cu(II), Co(II) and Ni(II) have been determined in aqueous medium at 313.15 K in the presence -and in the absence of I = 0.1 mol/L of NaCl.



A



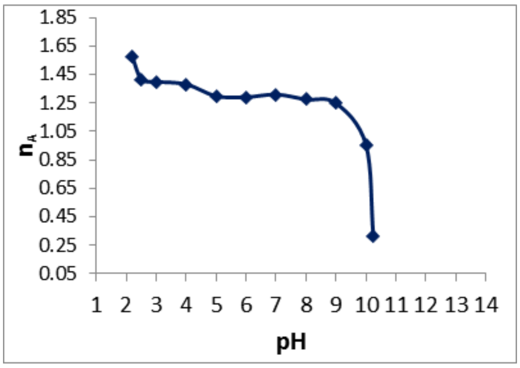
B

Fig. 2. Potentiometric titration curves of L-Valine - metal ions (II) complexes. A)- L-Valine-metal ions (II) complexes at 313.15 K in the absence ionic strength, B)- L-Valine - metal ions (II) complexes at 313.15 K and in the presence ionic strength.

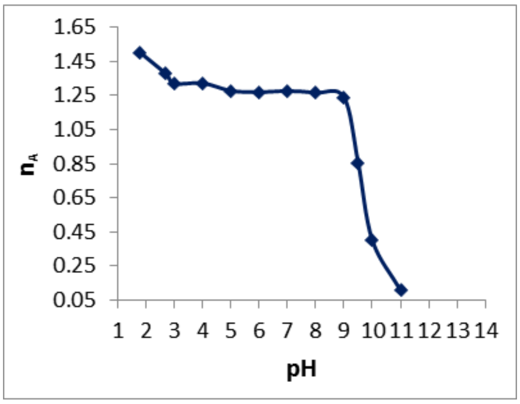
From (Fig. 2) the titration curves indicate that the ligand curve is slightly shifted to the left of the acid titration curve at lower pH value. The shift is due to the interaction of proton with the ligand and then with the metal ion. The values of n_A, (the degree of formation of the proton complex) were calculated [16, 18] by employing the following Equation 1:

$$n_A = Y + \left[(V' - V'')\times(N - E^\circ)\right] / \left[(V^\circ + V')\times T_L{}^\circ\right] \text{........ } (1)$$

Where Y=number of replaceable hydrogen ion, V°=total volume 50ml, V'=volume of alkali required by the acid, V"=volume of alkali used by acid and ligand, N=concentration of alkali, E°=total strength of acid, $T_{L°}$=total concentration of ligand.
The proton ligand formation curve was obtained by plotting the degree of formation (n_A) of the proton complex against pH values. The values of log K_1H and log K_2H were determined from the curves corresponding to n_A values of 0.5 and 1.5 (Fig. 3). The protonation constants at 313.15±0.1 K were calculated[18, 19] and summarized in Table **1.**



A



B

Fig. 3: pH-n_A curves for L-Valine, **A)**- at 313.15K and in the absence ionic strength, **B)**- at 313.15 K and in the ionic strength.

The values of ñ (average number of ligand molecules attached per metal ion) were calculated using equation (2)

$$\tilde{n} = \left[(V''' - V'')\times(N \times E^\circ)\right] / \left[(V^\circ + V'')\times n_A \times T_M{}^\circ\right] \text{......} (2)$$

Where V''' = volume of alkali used for acid + ligand + metal ion, $T_{M°}$ = total concentration of the metal ion, rest of term symbols are as given in equation (1). The free ligand exponent, pL was calculated using equations (b3) as given below [13, 14]

$$pL = \log_{10}\left\{\sum_{j=0}^{j=J} {}^{O}\beta_j{}^{H}[H]^j / (T_L - \bar{n}T_M)\right\} \text{.........} (a3)$$

$$pL = \log\left[\frac{1 + pk_1{}^H(1/\text{anti}\log\beta) + Pk_1{}^H(1/\text{anti}\log\beta)^2}{T_L{}^o - \bar{n}T_M{}^o}\,\frac{V^o + V^{III}}{V^o}\right] \text{....} (b3)$$

Where β_j^H = proton ligand stability constant, other term symbols are same as in Equation 1 and 2. log K_1 and log K_2 values were also obtained by Bjerrum half-integral method [16, 18] interpolation at half n values calculation method using the following equations:

$\log K_1 = pL$

$\log K_2 = pL$

It means if we plot a graph between ñ and pL (Fig. 4), then the corresponding values of pL at ñ equal to 0.5 and 1.5 gives log K_1 and log K_2 respectively.
strength
The values of logK_1 and logK_2 have also been determined in the absence and in the presence the ionic strength 0.10 M (NaCl) and they are summarized in Table1. The values of n obtained for metal-ligand system indicates the formation of 1:1 and 1:2 complexes. The overall order of stability (log β) is Cu(II)>Ni(II)>Co(II), this order is in accordance with Irving-Williams order of stability [17]. The values of listed Table 1 are related to the following equilibrium:

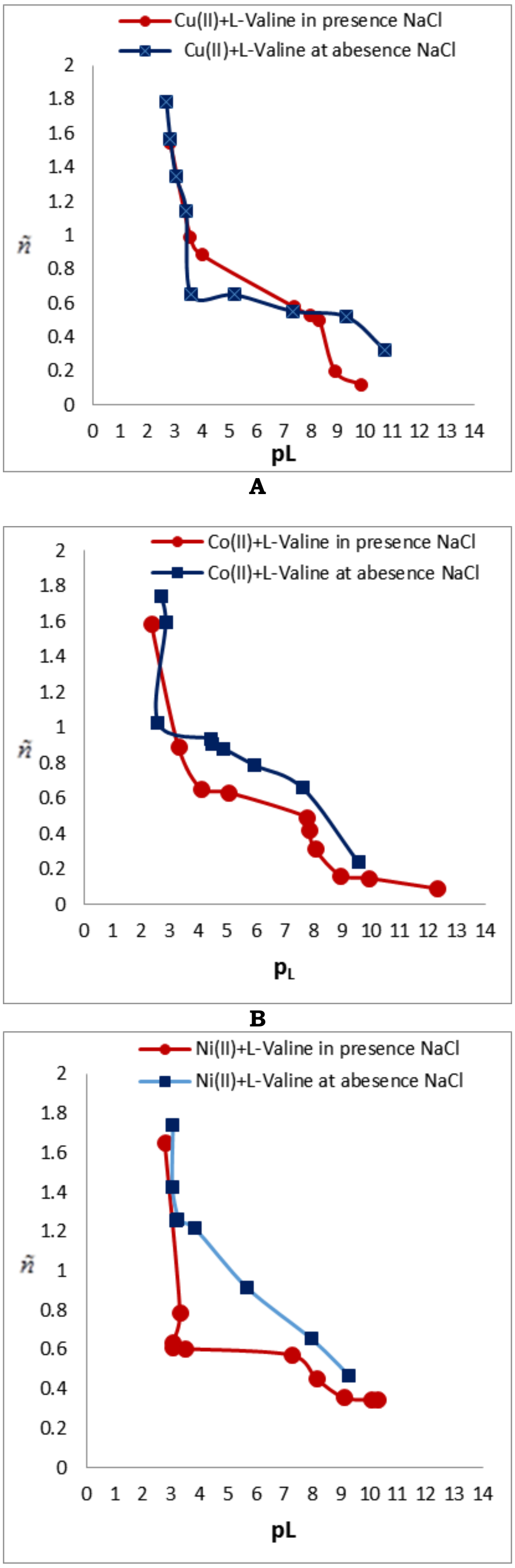
$H^+ + L^- \leftrightarrow HL$ $K_1 = [HL]/\ [H^+][L^-]$ 4a

$H^+ + HL^- \leftrightarrow H_2L$ $K_2 = [H_2L]/\ [H^+][HL^-]$ 4b

The $\log_{10}K_1$ value is associated to the attachment of proton to the NH_2-group in L-Valine and $\log_{10}K_2$ value corresponds to the protonation of α-carboxylate group. They show the logarithm of the formation constants for all types of complexes.

formation constants have been identified using potentiometric titration as given by the following equilibria 5a, 5b

$$M+L \longleftrightarrow ML \qquad K_1=[ML]\ /\ [M][L] \ ....5a$$
$$M+2L \longleftrightarrow ML_2 \qquad K_2=[ML_2]\ /\ [M][L]^2 \ ....5b$$



A

B

C

Fig. 4: plot of $\bar{n}$ against (pL) at 313.15 K in the absence and in the presence of ionic strength: A) Cu(II), B) Co(II) and C) Ni(II)

Table 1: Protonation constants of L-Valine and stability constants of its complexes in the absence and in the presence 0.1M NaCl (Ionic strength)

Ion strength	Species	Log K_1	Log K_2	Logβ_2
Absence 0.1M NaCl	L-Val	2.314	*10.123*	*12.437*
	Co(II)	2.789	*8.399*	*11.188*
	Ni(II)	2.866	*8.756*	*11.622*
	Cu(II)	2.995	*9.342*	*12.337*
Presence 0.1M NaCl	L-Val	2.298	*9.805*	*12.103*
	Co(II)	2.495	*7.674*	*10.169*
	Ni(II)	2.859	*7.829*	*10.688*
	Cu(II)	2.957	*8.369*	*11.326*

in Addition, the perusal of this data shows that the values of Protonation constants of L-Valine decreases in the presence of ionic strength, so the degree of dissociation of ligand decreases. There is a decrease in the stability constants of the complexes of these metal ions with ligand compared to the results of the stability constants without ionic strength, which it indicated to an increase in bonding between the metal and the bonds of these complexes in the absence ionic strength.

Conclusion

The results of the potentiometric studies on complexes of L-Valine with Co(II), Ni(II) and Cu(II) indicate that the order of stability is Cu(II) > Ni(II) > Co(II). This order is in accordance with Irving-Williams order of stability. The values of stability constants in the absence of 0.1M NaCl ionic strength are higher than the values of stability constants in the presence 0.1M NaCl ionic strength.

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References

[1]- M. Cempel, Nikel, G. , "Nickel: A Review of Its Sources and Environmental Toxicology," *Polish Journal of Environmental Studies,* vol. 15, pp. 375-382, 2006.

[2]- Q. A. Acton, *Branched-Chain Amino Acids: Advances in Research and Application*: ScholarlyEditions, 2013

[3]- R. Alexandrova, Rasshkova, G., Alexandrov, I., Tsenova, W., Tudose, R. and Costisor, O. , "Briefly about copper," *Experim. Pathol. and Parasitol.*, vol. 2003, pp. 1311, 6851, 2003.

[4]- B. G. Malmström and J. Leckner, "The chemical biology of copper," *Current Opinion in Chemical Biology*, vol. 2, pp. 286-292, 1998/04/01/ 1998.

[5]- N. Coleman, *et al.*, *The Toxicology of Essential and Nonessential Metals*: Lulu.com, 2017.

[6]- R. M. Smith, *et al.*, "Prediction of stability constants. II. Metal chelates of natural alkyl amino acids and their synthetic analogs," *Inorganica Chimica Acta,* vol. 103, pp. 73-82, 1985/09/02/ 1985.

[7]- A. Gergely*, et al.*, "Thermodynamic relations of parent and mixed complexes of asparagine and glutamine with copper(II)," *Journal of Inorganic and Nuclear Chemistry,* vol. 37, pp. 551-555, 1975/02/01/ 1975.

[8]- "IUPAC-IUB Joint Commission on Biochemical Nomenclature (JCBN). Nomenclature and symbolism for amino acids and peptides. Recommendations 1983," *Biochemical Journal,* vol. 219, pp. 345-373, 1984.

[9]- C. J. Lynch and S. H. Adams, "Branched-chain amino acids in metabolic signalling and insulin resistance," *Nature Reviews Endocrinology,* vol. 10, p. 723, 2014.

[10]- B. E. Leach and R. J. Angelici, "Stereoselective interaction of optically active amino acids and esters with (L;valine-N-monoacetato)copper(II)," *Journal of the American Chemical Society,* vol. 91, pp. 6296-6300, 1969/11/01 1969.

[11]- Y. Masaaki, Shingo, Kikuchi,Jun, Sen, Toshimichi, Kamei, Norihito, Doki, "Cu(II) Complex of L-Leucine Favor a Different Type of Crystal Structure from Cu(II)-L-Val and Cu(II)-L-Ile," *Advances in Chemical Engineering and Science,* vol. 6, p. 5.

[12]- V. A. a. M. Davankov, P. R., "Stereoselectivity in bis(α-amino-acid)copper(II) complexes," *Journal of the Chemical Society, Dalton Transactions,* vol. 168, p. 1012, 1972.

[13]- [13] L. Antolini*, et al.*, "Silver(I) complexes with N-protected amino acids," *Inorganica Chimica Acta,* vol. 46, pp. L77-L78, 1980/01/01/ 1980.

[14]- R. K. Singh S., Ranjit, "Complexation reaction of metal ions with peptide systems. VII. Equilibrium studies of N-benzoyl-L-valine, N-benzoyl-glycyl-L-valine and isovaleric acid with metal(II) ion systems," *Thermochimica Acta,* vol. 40, pp. 305-309, 1980/09/15/ 1980.

[15]- J. Bjerrum, *Metal ammine formation in aqueous solution: theory of the reversible step reactions*: P. Haase, 1957.

[16]- J. BJERRUM, *Stability Constants of Metal-Ion Complexes with Solubility Products of Inorganic Substances. Stability Constants of Metal-Ion Complexes. Section I: Inorganic Ligands. Compiled by Lars Gunnar Sillén. Section II: Organic Ligands. Compiled by Arthur E. Martell ... Second Edition, Etc*, 1964.

[17]- H. W. Irving, R. J. P., "The stability of transition-metal complexes," *Journal of the Chemical Society (Resumed),* vol. 637, pp. 3192-3210, 1953.

[18]- H. M. Irving and H. S. Rossotti, "The calculation of formation curves of metal complexes from pH titration curves in mixed solvents," *Journal of the Chemical Society (Resumed),* vol. 638, pp. 2904-2910, 1954.

[19]- H. M. R. Irving, H. S., "Methods for computing successive stability constants from experimental formation curves," *J Chem. Soc,* vol. 75, pp. 3397-3405, 1953.