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Thermodynamic and kinetic Calculation for the Binding of Nickel (II) with Some Chelating Agents

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Abstract

Chelating agents were used in a chelation therapy to detoxify heavy metals and toxins and convert them to an inactive form which was excreted out of the body. Nickel is one of these toxic heavy metal when presented in a high values over its allowable limit. This work studies the complexation of some amino acid (Glycine, Histidine, and Arginine) with nickel (II) ion and compare the result with complexation of EDTA (the synthesized amino acid) used in the chelation therapy. Our experiment were performed in a phosphate buffer of PH (7.2) and in a different temperature (283, 288,293, 298, 303)K . The results show a high tendency for these amino acid to nickel ion with an equilibrium constant in arrange of [$K_{Ni(II)-EDTA}(17.2\times10^{8}) > K_{Ni(II)-Gly}(29\times10^{6}) > K_{Ni(II)-His}(9\times10^{6}) > K_{Ni(II)-Arg}(4.57\times10^{6})$] $mol^{-1}.L$. The thermodynamic parameter indicate a spontaneous interaction (negative free energy change $\Delta G°$)) and was positive for each of the enthalpy (ΔH^{0}) and entropy (ΔS^{0}) values indicate that the nature of the emotion is a strong hydrophobic and electrostatic forces, and a second order interaction kinetics with a rate constant in a range of [$(6,8\times10^{-2})$, (11.9×10^{-2}), (21×10^{-2}), (21.8×10^{-2})] $M^{-1}.min^{-1}$each (EDTA, Arginine, Histidine, Glycine) respectively .

Keywords: kinetic parameters, thermodynamic parameters, Ni (II), EDTA, Amino acid

حسابات ثرموداينميكية وحركية لارتباط ايون النيكل الثنائي مع بعض العوامل الكلابية

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الخلاصة

العلاج بالاستخلاب عبارة عن اسبخدام عوامل مخلبية لازالة سموم المعادن الثقيلة وتحويلها الى شكل غير فعال والتي يتم افرازه بدون اي تاثير جانبي على الجسم ، يعتبر النيكل من العناصر الانتقالية الثقيلة ذات التاثير السمي عند ازدياد نسبته عن الحد المسموح به ، يتضمن العمل دراسة ارتباط ايون النيكل الثنائي مع بعض الاحماض الامينية (كلايسين، هستيدين، ارجنين) ومقارنة نتائج ارتباطه وتكوين المعقد مع EDTA (والذي يعتبر من الاحماض الامينية المصنعة) والمستعمل في العلاج الكلابي. التجربة اجريت في المحلول الفوسفاتي ذو القوة الهيدروجينية (7.2) وفي درجات حرارية مختلفة, (283, 288, 293, 298, 303) كلفن. النتائج اظهرت ميل كبير لارتباط الاحماض الامينية (EDTA، الكلايسين، الهستيدين، الارجنين) مع ايون النيكل الثنائي وحسب ثوابت التوازن المترتبة تصاعديا" [$K_{Ni-EDTA}(17.2\times10^{8}) > K_{Ni-Gly}(29\times10^{6})$ > $K_{Ni-His}(9\times10^{6}) > K_{Ni-Arg}(4.57\times10^{6})$] مول$^{-1}$.لتر. ان الدوال الثرموداينميكية تدل على التأثر

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التلقائي من خلال القيمة السالبة للطاقة الحرة لكبس وان القيمة الموجبة لكل من الانثالبي (ΔH^0) والانتروبي (ΔS^0) تدل على ان طبيعة التاثر عبارة عن قوى هيدروفوبية والكتروستاتيكية, وان التفاعل من المرتبة الثانية وحسب ثوابت السرعة وضمن المدى [(21.8×10^{-2}), (21×10^{-2}), (11.9×10^{-2}), (6.8×10^{-2})] مول$^{-}$ ^{1}دقيقة$^{-1}$ لكل من(EDTA، الارجنين، الهستدين، الكلايسين) على التوالي.

Introduction

Chelation: Describes a particular way that ions and molecules bind metal ions [1]. It involves the formation or presence of two or more separate coordinate bonds between a polydentate (multiple bonded) ligand and a single central atom [2]. Usually these ligands are organic compounds, and are called chelants, chelators, chelating agents, or sequestering agents [3].

Chelation therapy: is a medical procedure that involves the administration of chelating agents to remove heavy metals from the body [4]. Heavy metal intoxication with the administration of chelating agent forms a stable complex with the toxic heavy metal species and prevents them from attacking biological to gets; Chelation therapy has a long history of use in clinical toxicology. [5] And remains in use for some very specific medical treatments, although it is administered under very careful medical supervision due to various inherent risks [6].

Chelation therapy must be administered with care as it has a number of possible side effects.[5] In response to increasing use of chelation therapy as alternative medicine and in circumstances in which the therapy should not be used in conventional medicine, various health organizations have confirmed that medical evidence does not support the effectiveness of chelation therapy for any purpose other than the treatment of heavy metal poisoning [7, 8].

The first example of chelation therapy dates back to 1941 when kety et al tried to use sodium citrate to treat lead poisoning [9]. After that, more effective heavy metal chelating agents have been developed for detoxification of heavy metal poisoning.

In 1947 a synthetic amino acid called ethylene-diamine-tetra acetic acid (EDTA) was approved by the Food and Drug Administration (FDA) as a safe additive [10].

EDTA is the best of chelation agents and it used of higher rang to riding from toxics of a heavy metals and it was widely used to dissolve lime scale. Its usefulness arises because of its role as a hexadentate ("six-toothed") ligand and chelating agent, i.e., its ability to "sequester" metal ions such as Ca^{2+} and Fe^{3+}. After being bound by EDTA, metal ions remain in solution but exhibit diminished reactivity. EDTA is produced as several salts, notably disodium EDTA and calcium disodium EDTA with metal figure-1 [11, 12].

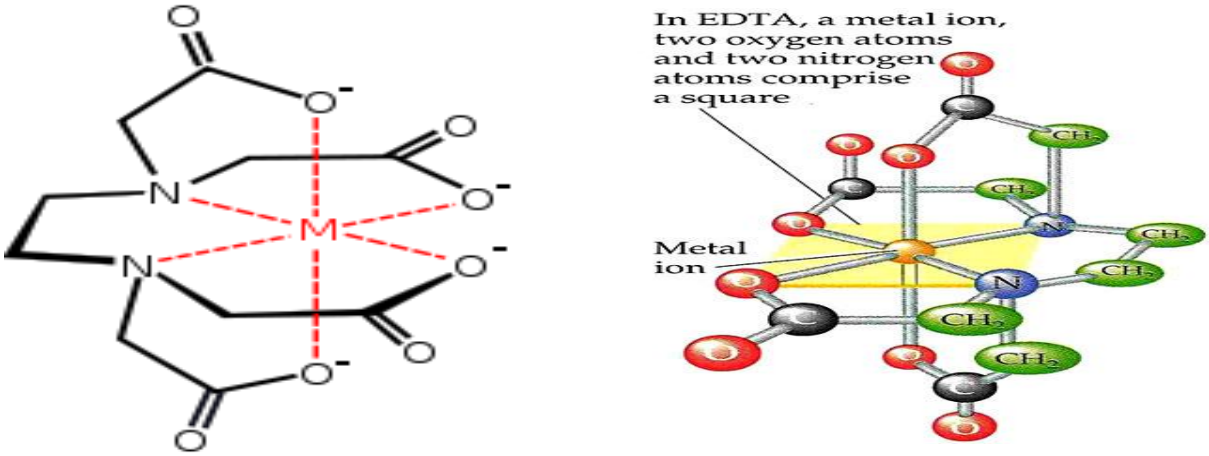


Figure1-Structures shows that binding EDTA with a heavy metal [11,12]

Nickel (II): is an environmental carcinogen, nephrotoxic and hepatotoxic heavy metal [13, 14]. As for most metals, the toxicity of nickel is dependent on the route of exposure and the solubility of the nickel compound [15]. The genotoxic effects of nickel might be prevented by some exogenous supplementation [16].

Our present study involves a thermodynamic and kinetic calculation for the interaction of amino acids (Glycine, histidine, and arginine) as a chelators with Nickel (II); which is one of the toxic heavy metal, and a comparison with EDTA as a chelators with the same ion.

Experimental

Reagent and chemicals: A standard solution of sodium hydroxide (NaOH), [M.Wt(40g.mol^{-1}), Fluka, 4M] was prepared by dissolving (16g) in 100ml double distilled water.

A stock solution (10^{-2}M) of EDTA [$C_{10}H_{16}N_2O_8$, M.Wt(242.25g.mol-1),LOBA chemie/india] was Prepared by dissolving (0.2922g) in 100ml double distilled water, with the addition of two drops of 4M NaOH solution.

A stock solution of Nickel nitrate [$Ni(NO_3)_2.6H_2O$, M.Wt(290.81g.mol^{-1}), analar/England, (10^{-2} mol.L^{-1})] was prepared by dissolving (0.290g) in 100ml distilled water.

A stock solution of (10^{-2}M)amino acids{[Glycine; $C_2H_5NO_2$, M.Wt(75.066g.mol^{-1}), Histidine; $C_6H_9N_3O_2$, M.Wt(155.15g.mol^{-1}), Arginine; $C_6H_{14}N_4O_2$, M.Wt(174.2g.mol^{-1})] all from Fluka/ Switzerland} were prepared by dissolving (0.075g, 0.155g, 0.174g) respectively ,in 100 ml distilled water for each one.

Phosphate buffer solution: A series of phosphate buffer solution of pH values (5.7, 6.5, 7.2, 8.0) were prepared by placing definite volume of mono basic sodium phosphate [$NaH_2PO_4.2H_2O$, M.Wt(156.01g.Mol^{-1}), Merck/Germany; (0.2M)] in to 200 ml volumetric flask and completed to the mark with a solution of di basic sodium phosphate[$Na_2HPO_4.2H_2O$, M.Wt(177.99g.Mol^{-1}), Fluka AG/Switzerland, (0.2M)] to obtain the required pH values [17,18].

Absorption spectroscopy: All spectral measurements were recorded on a double beam UV-Visible spectrophotometric, shimadzue – model UV-1800, using a 1cm path length quartz cell. Absorbance value of Ligands in the presence and absence of Ni (II) solution were made in the range of (190-600nm).

Stoichiometric analysis: The stoichiometry of the complexion of ligands with Ni (II) ion was determined by continuous variation method (Jobs method) [19,20] Eqimolar concentrations (10^{-4}M) of a ligand and Ni $(NO_3)_2$ were prepared, Job method was applied by placing 1 to 9 ml of (10^{-4}M) ligands solution into series of 10 ml flask, this was followed by placing 9 to 1 ml of (10^{-4}M) Ni $(NO_3)_2$ solution, and the absorbance were measured at the maximum wave length.

Results and discussion

Absorption spectroscopy: The optimized pH of a phosphate buffer was obtained by measuring the UV-Vis absorption spectra of nickel (II) solution in a phosphate buffer as a solvent .Table-1 shows their wave length and absorbance, and it is obvious that the best PH is (7.2).

Table 1-Electronic spectra data of ($1*10^{-2}$M) Ni (II) in different pH values of phosphate buffer.

pH	λmax/nm	Absorbance
5.7	215	3.194
6.5	215	3.286
7.2	216	3.316
8.0	216	3.273

The UV-Vis absorption spectra of the studied amino acid (Glycine, Histidine, Arginine ,and EDTA)were measured in a phosphate buffer of PH (7.2) .

Figure-1 shows the electronic spectra of these amino acids and their structure . amino acid peaks attributed to ($\pi \longrightarrow \pi^*$) and (n $\longrightarrow \pi^*$) transitions [21,22].

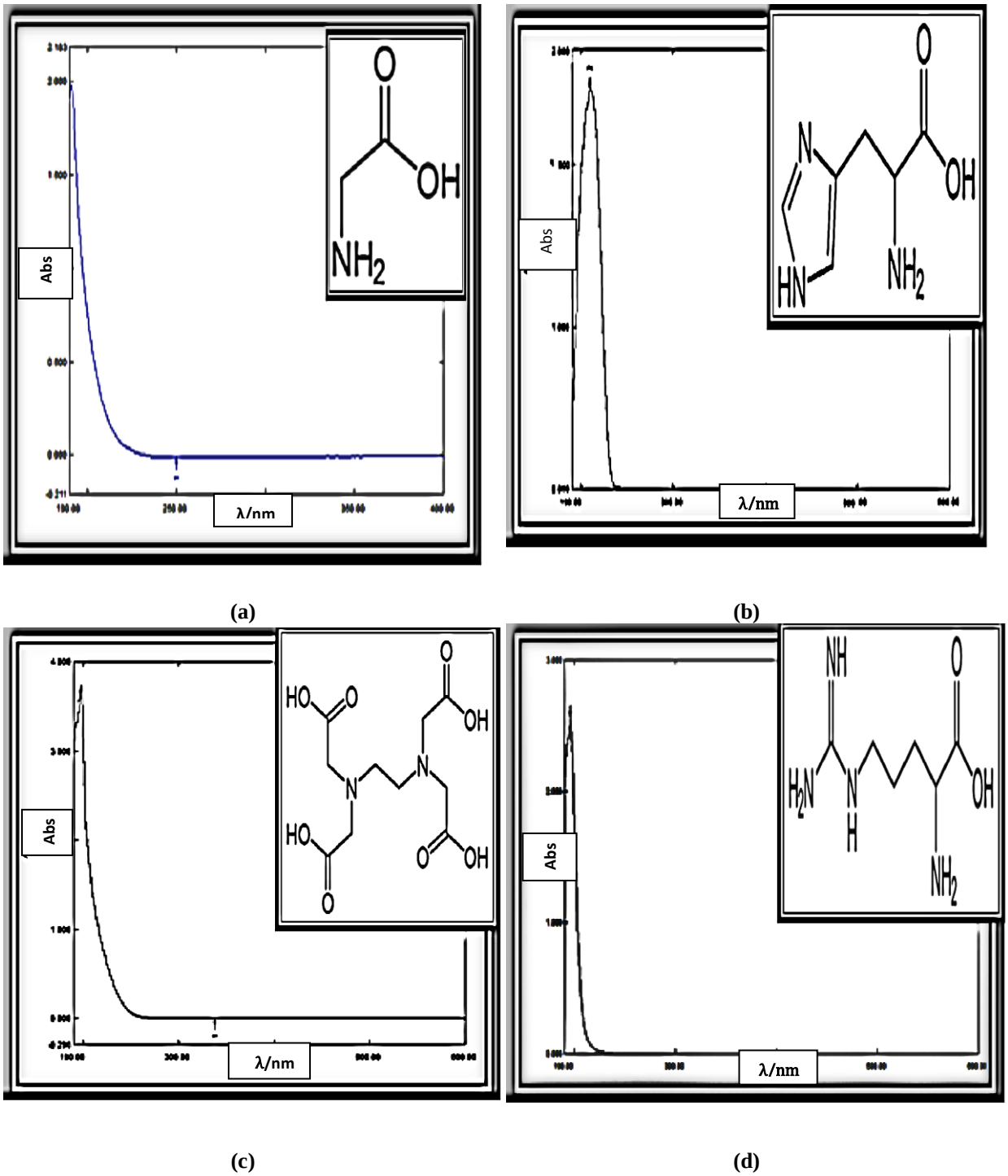


Figure 1-UV-Visible absorption spectra of ($4*10^{-4}$M) amino acid in phosphate buffer of (pH=7.2). **(a)** Glycine, **(b)** Histidine, **(c)** EDTA, **(d)** Arginine**.**

Upon the addition of nickel (II) to amino acid solution, a signification change were observed in their electronic spectra, these spectra shows a shift in the λ_{max} to a longer wave length (bathochromic shift) and a change in their absorbance and the appearance of a new peak in a longer wave length, these two evidence indicate a complex formation between the studied amino acid and nickel (II). Figure -2 illustrate the electronic spectra of a mixture of amino acid with nickel(II).

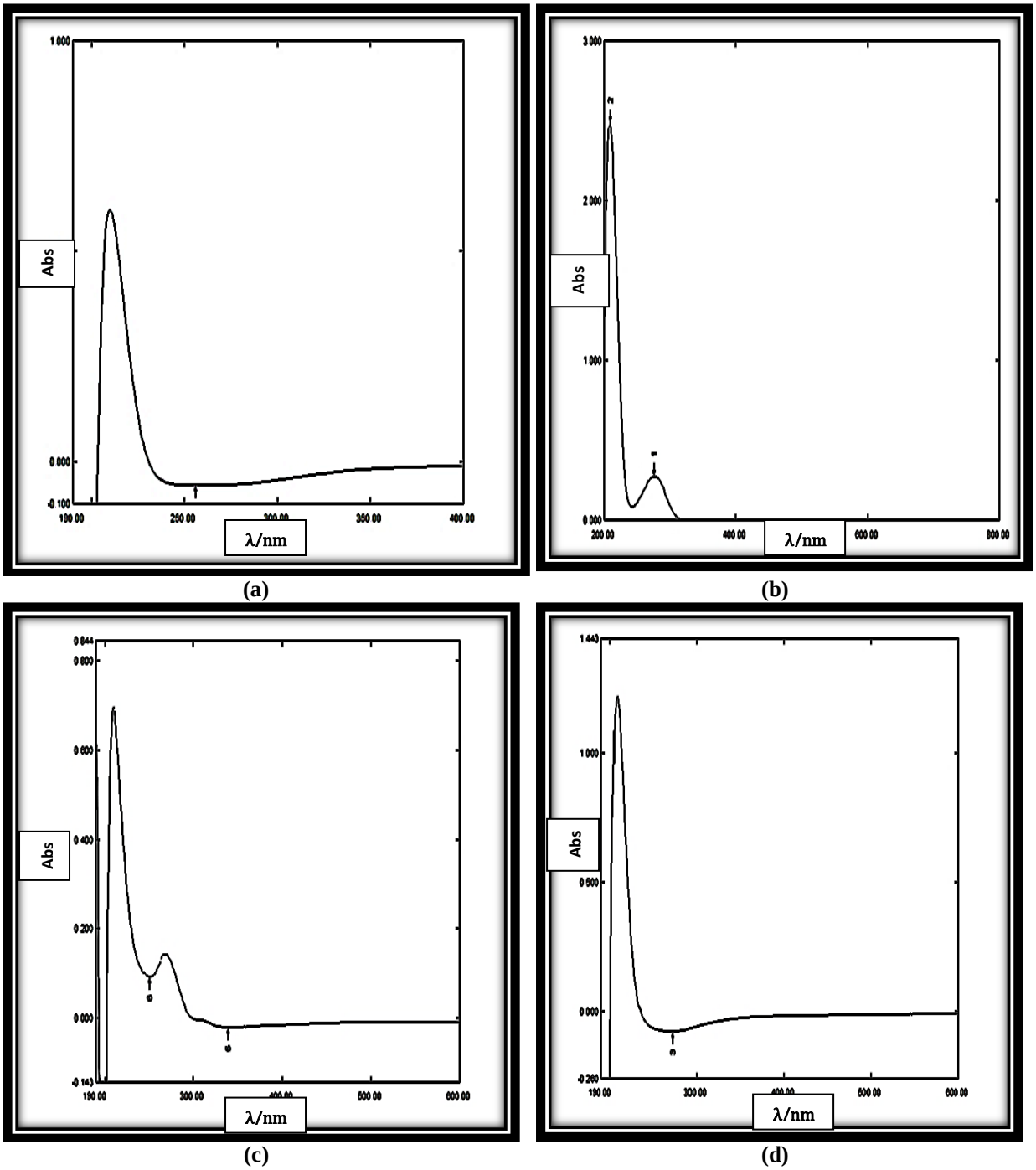


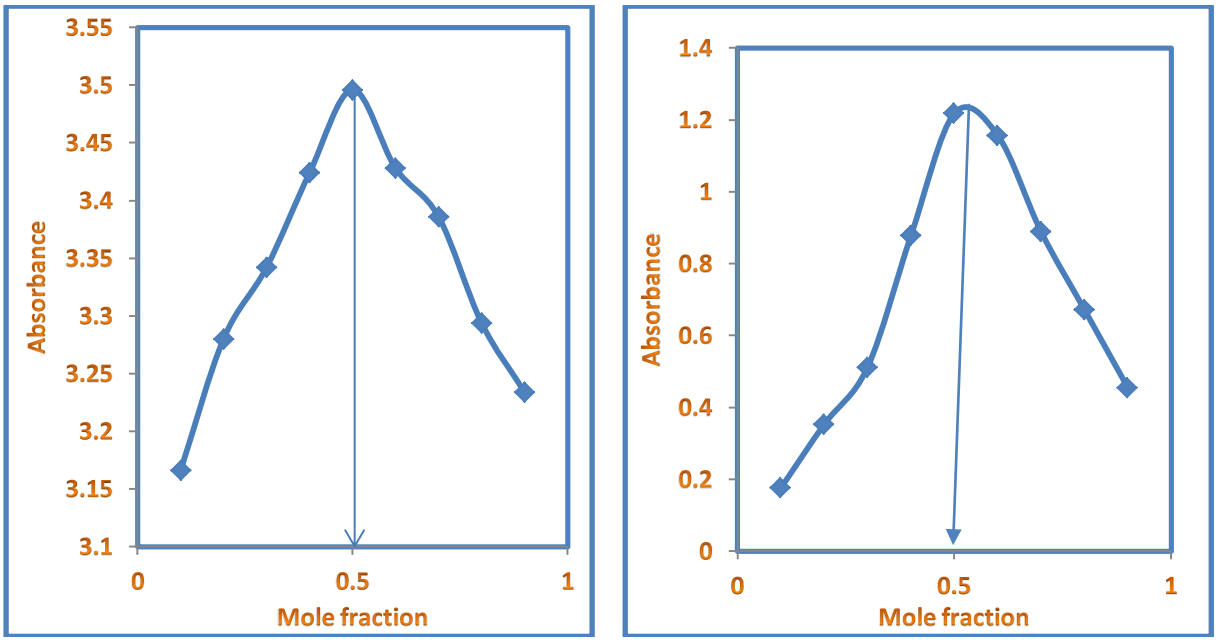
Figure 2- UV-Vis absorption spectra of a mixture of amino acid and Ni (II) at phosphate buffer of (pH=7.2) **(a)** Glycine + Ni(II) **(b)** Histidine + Ni(II) **(c)** Arginine + Ni(II) **(d)** EDTA + Ni(II)

Table-2 illustrates their wave length and absorbance for amino acid alone and with the addition of nickel (II).

Table 2-Electronic spectra of (4*10-4M) amino acid in phosphate buffer of pH (7.2) and their mixture with nickel (II).

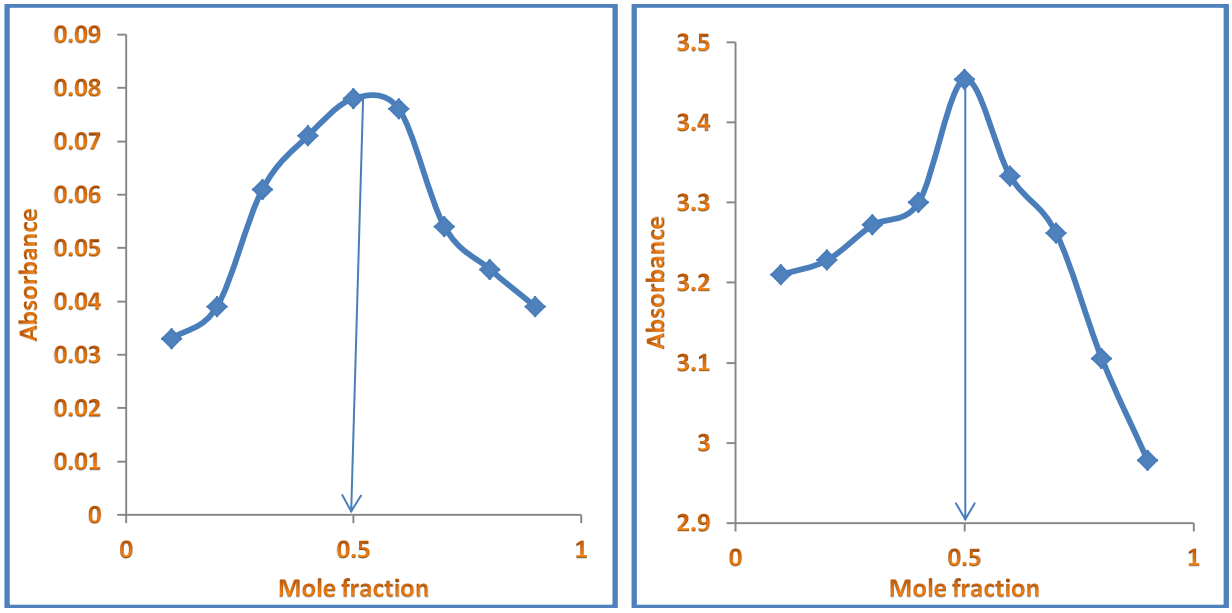
NO	Compound	λ_{max}/ nm	Absorbance	$\Delta\lambda_{max}$/nm	Assignment
1	Glycine	191	1.783		$\pi \rightarrow \pi$
1.b	Glycine + Ni(II)	216	0.599	25	$\pi \rightarrow \pi$
2	Histidine	210	1.845		$\pi \rightarrow \pi$
2,b	Histidine +Ni(II)	210 277	2.571 0.234	67	$\pi \rightarrow \pi$ $n \rightarrow \pi$
3	Arginine	196	2.566		$\pi \rightarrow \pi$
3.b	Arginine + Ni(II)	208 270	0.695 0.143	12 74	$\pi \rightarrow \pi$ $n \rightarrow \pi$
4	EDTA	194	2.929		$\pi \rightarrow \pi$
4.b	EDTA + Ni(II)	214	1.217	20	$\pi \rightarrow \pi$

Stoichiometric analysis: The stoichiometry of the complex of nickel (II) with amino acids (Glycine, Histidine, Arginine, EDTA) were calculated by the method of continuous variations (Job method) of equimolar solution [23]. The curve displayed maxima absorbance at mole fraction (V1/V1+V2), X_{max} = 0.5, which indicates the formation of complex with metal ion to ligand ratio (1:1), figure-3(a,b),-4(a,b). $n = X_{max} / 1 - X_{max}$, n represent coordination number of the complex, X_{max} represent mole fraction corresponding to the maxima absorbance.



(a) **(b)**

Figure 3- Job's plot for the composition of Ni (II) with (a) Glycine at λ=216 nm and PH (7.2) at (298K), (b) Histidine at λ=277 nm and PH (7.2) at (298K).



(a) **(b)**

Figure 4- Job's plot for the composition of Ni (II) with (a) Arginine at λ=270 nm and pH(7.2) at (298k), (b) EDTA at λ=214 nm and pH(7.2) at (298K).

Stability constant (Keq): The equilibrium constant can be calculated using the continuous variation method. [24]

$$Ni\ (II) + ligand \rightleftharpoons [Ni\ (II) - ligand]_{complex}$$

$$K_{eq} = \frac{[(Ni(II)-ligand)complex]eq}{[Ni(II)]eq\ [ligand]eq} \quad \text{..... (1)}$$

$$K_{eq} = \frac{[A_{max}/\varepsilon l]}{[C_{Ni} - A_{max}/\varepsilon l]\,[C_{ligand} - A_{max}/\varepsilon l]} \quad \text{..... (2)}$$

A_{max} = the maximum absorbance of the complex
ε = molar absorptivity of the complex (L. mole^{-1}. cm^{-1})
l = path length. cm.
C_{Ni} = Initial concentration of the metal ion.
C_{ligand} =Initial concentration of amino acid.

$[(Ni(II)\text{-}ligand)_{complex}]_{eq}$ = Absorbance(max)/εl ..... (3)

$[Ni(II)]_{eq} = [Ni(II)_0 - [(Ni(II)\text{-}ligand)_{complex}]_{eq}]$ ..... (4)

$[ligand]_{eq} = [ligand]_0 - [(Ni(II)\text{-}ligand)_{complex}]_{eq}]$ ..... (5)

The molar absorptivity of the complex was calculated by recording the absorbance of a various concentration of the (1:1) complex and plotting of the absorbance of the complex against concentration given a straight line with the slope equal to ($\mathcal{E}$), ε = mole^{-1}. cm^{-1}.The values of **k**eq obtained by the continuous variation method were determined in five temperatures (283 - 303K) as shown in Table -3.

Table 3- Equilibrium constant of Nickel (II)- amino acid complex at different temperature.

Sample No.	Temp. (K)	Keq(Ni(II)-Gly)complex $mol^{-1}.L$	Keq(Ni(II)-His)complex $mol^{-1}.L$	Keq(Ni(II)-Arg)complex $mol^{-1}.L$	Keq(Ni(II)-EDTA)complex $mol^{-1}.L$
1	283	3.80×10^6	1.70×10^6	1.50×10^6	1.40×10^8
2	288	7.00×10^6	3.20×10^6	2.10×10^6	4.50×10^8
3	293	13.3×10^6	5.60×10^6	3.00×10^6	7.96×10^8
4	298	29.0×10^6	9.00×10^6	4.57×10^6	17.2×10^8
5	303	60.0×10^6	16.7×10^6	6.40×10^6	41.2×10^8

Table -3 shows the dependence of equilibrium constant with temperature, it increases with the increase in temperature, which means the stability of the complex increase with temperature.

Thermodynamic Parameters: the enthalpy changes ΔH^0, the entropy changes ΔS^0 and the free energy changes ΔG^0, have been reported of the complextion (Ni (II) - amino acid) in table- 4, 5, 6, 7.

Table 4- Thermodynamic parameters for Ni (II)-glycine complex, at PH(7.2)

T(K)	Ln k_{eq}	$\Delta G^0(J.mol^{-1})$	$\Delta H^0(J.mol^{-1})$	$\Delta S^0(J.mol^{-1}.K^{-1})$
283	15.15	-35647.06	100998.4	482.8
288	15.76	-37743.06	100998.4	481.7
293	16.40	-39958.4	100998.4	481.08
298	17.2	-42571.6	100998.4	481.77
303	17.9	-45117.46	100998.4	482.2

Table 5- Thermodynamic parameters for Ni (II)-histidine complex, at PH(7.2)

T(K)	lnK_{eq}	$\Delta G^0(J.mol^{-1})$	$\Delta H^0(J.mol^{-1})$	$\Delta S^0(J.mol^{-1}.K^{-1})$
283	14.35	-33754.48	81345	406.71
288	14.98	-35865.38	81345	406.98
293	15.46	-37670.74	81345	406.19
298	16.00	-39672.70	81345	406.09
303	16.63	-41895.64	81345	406.73

Table 6- Thermodynamic parameters for Ni (II)-Arginine complex, at PH(7.2)

T(K)	lnK_{eq}	$\Delta G^0(J.mol^{-1})$	$\Delta H^0(J.mol^{-1})$	$\Delta S^0(J.mol^{-1}.K^{-1})$
283	14.22	-33459.99	53565.4	307.5
288	14.55	-34856.81	53565.4	307.02
293	14.91	-36330.8	53565.4	306.81
298	15.33	-37993.62	53565.4	307.24
303	15.67	-39479.51	53565.4	307.07

Table 7- Thermodynamic parameters for Ni (II)-EDTA complex, at PH(7.2)

T(K)	lnK_{eq}	$\Delta G^0(J.mol^{-1})$	$\Delta H^0(J.mol^{-1})$	$\Delta S^0(J.mol^{-1}K^{-1})$
283	18.76	-44132.9	118183.5	573.5
288	19.92	-47708.4	118183.5	576.01
293	20.49	-49926.1	118183.5	573.75
298	21.26	-52687.03	118183.5	573.39
303	22.14	-55771.58	118183.5	574.1

The enthalpy changes were calculated by substituting the value of the slope of the plot (*log Keq* vs *1/T*) in the vant Hoff equation (6), figure-5. [25]

$$\ln Keq = -\Delta H^o/_{RT} \quad \text{..... (6)}$$

$$Slope = -\Delta H^o/_{R}$$

R = gas constant.

The change in Gibbs free energy can be determined from equation (7), the relation between K_{eq} and ΔG^0 [26], and the entropy changes from equation (8).

$$\Delta G^o = -RT \ln Keq \quad \text{..... (7)}$$

$$\Delta G^o = \Delta H^o - T\,\Delta S^o \quad \text{..... (8)}$$

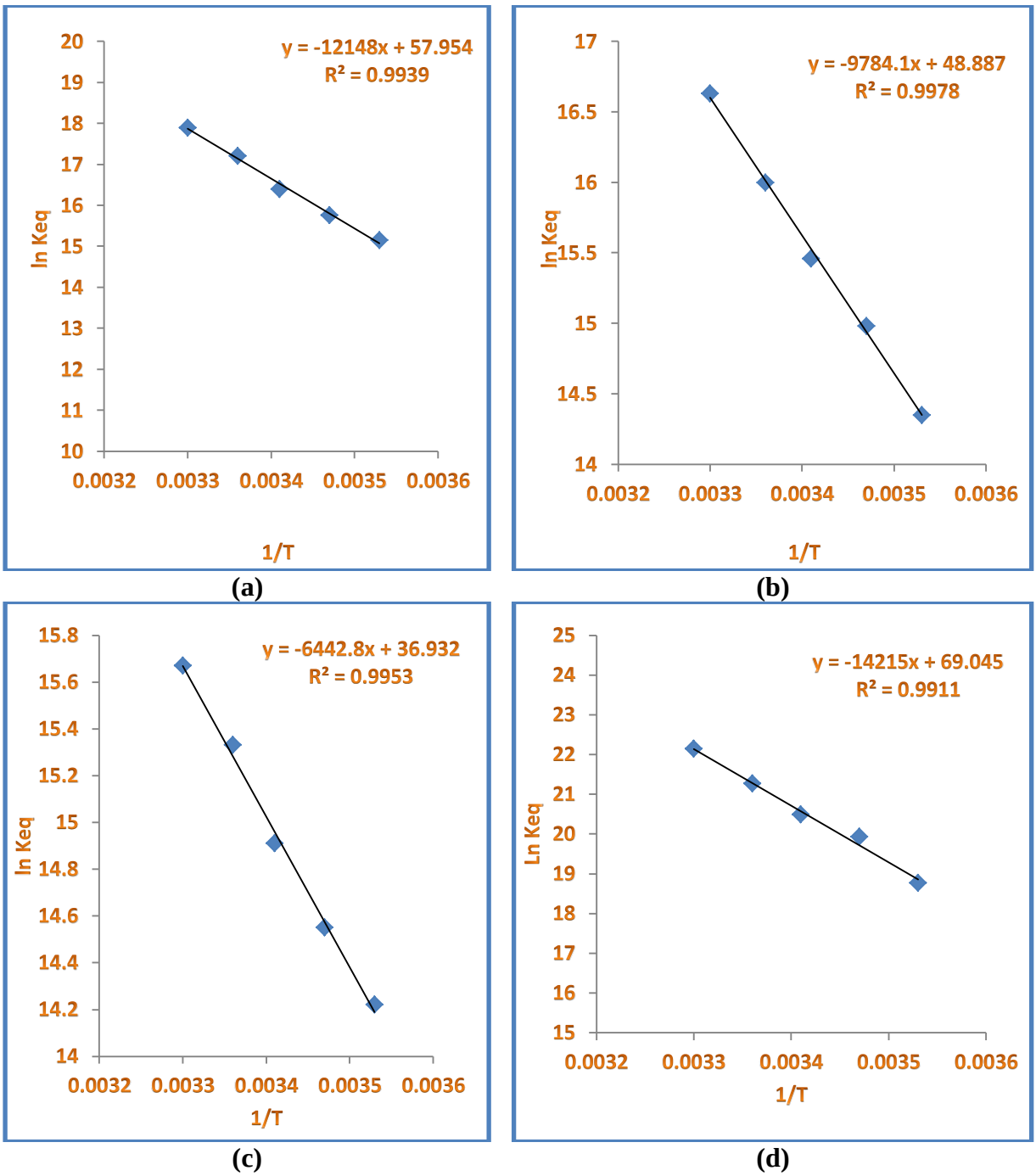


Figure 5- Vant Hoff plot for interaction of Nickel(II) with (a)Glycine (b) Histidine (c) Arginine (d) EDTA

Gibbs free energy is very importance in deciding the direction of process and position of equilibrium. The negative values of Gibbs free energy for these interaction indicates the spontaneous process in the direction of equilibrium and increase with the increase in temperature. The enthalpy of interaction has a positive value indicating that formation of ligand – Ni(II) complex is endothermic. The positive value of enthalpy and entropy change also refers to the type of interaction between ligand and Nickel (II) ion which are electrostatic in nature.

Interaction Kinetics: In order to investigate the interaction kinetic of nickel (II) ion with amino acids, the absorbance of (1:1) complexes were followed with time at a certain wave length.
The first order rate equation and the second order rate equation were applied.

$$A+B \longrightarrow C+D$$

k:rate constant for the reaction which is independent of the concentration but depends on the temperature.
First order reaction: The first order rate law for the consumptive of a reaction A:

$$\frac{dA}{dt} = -K[A] \quad \text{..... (9)}$$

$$ln\left(\frac{[A]}{[A]_o}\right) = -Kt \quad \text{..... (10)}$$

$$ln\, A - ln\, A_o = -Kt \quad \text{..... (11)}$$

Second order reaction: The second-order rate law**.**

$$\frac{d[A]}{dt} = -K[A]^2 \quad \text{..... (12)}$$

$$\frac{1}{[A]} - \frac{1}{[A]_o} = Kt \quad \text{..... (13)}$$

A= Absorbance of complex (Ni (II)-ligand) with deferent time.
$\mathbf{A_o}$ = Absorbance of complex (Ni (II)-ligand) in time zero.

Table -8, 9, 10, and 11 shows the absorption of complex Ni (II) with (Glycine, Histidine, Arginine, EDTA) all of each with Time (0-30) min.

Table 8- Data for application the second order equation for (1:1) Ni (II)-Gly complex, at 298K,$\lambda_{max=}$216nm.

Time (min)	Absorbance	1/A
0	0.17	5.882353
5	0.141	7.092199
10	0.129	7.751938
15	0.110	9.090909
20	0.098	10.20408
25	0.087	11.49425
30	0.081	12.34568

Table 9 - Data for application the second order equation for (1:1) Ni(II)-His complex, at 298K,$\lambda_{max=}$277nm.

Time (min)	Absorbance	1/A
0	0.261	3.831418
5	0.197	5.076142
10	0.175	5.714286
15	0.146	6.849315
20	0.123	8.130081
25	0.109	9.174312
30	0.099	10.10101

Table 10- Data for application the second order equation for (1:1) Ni (II)-Arg complex, at 298K,λ_{max}=270nm.

Time (min)	Absorbance	1/A
0	0.321	3.115265
5	0.278	3.597122
10	0.247	4.048583
15	0.217	4.608295
20	0.188	5.319149
25	0.167	5.988024
30	0.150	6.666667

Table 11-Data for application the second order equation for (1:1) Ni(II)-EDTA complex, at 298K,λ_{max}=214nm.

Time (min)	Absorbance	1/A
0	0.352	2.840102
5	0.321	3.115265
10	0.292	3.424658
15	0.262	3.816794
20	0.240	4.166667
25	0.223	4.484305
30	0.205	4.878049

A plot of (1/A) against time (t) was presented in figure-6 by the application of equation (13).A straight line were obtained which indicates the second order interaction between nickel(II) and these amino acids with a rate constant illustrated in table-12 which was calculated from the slope of the straight line.

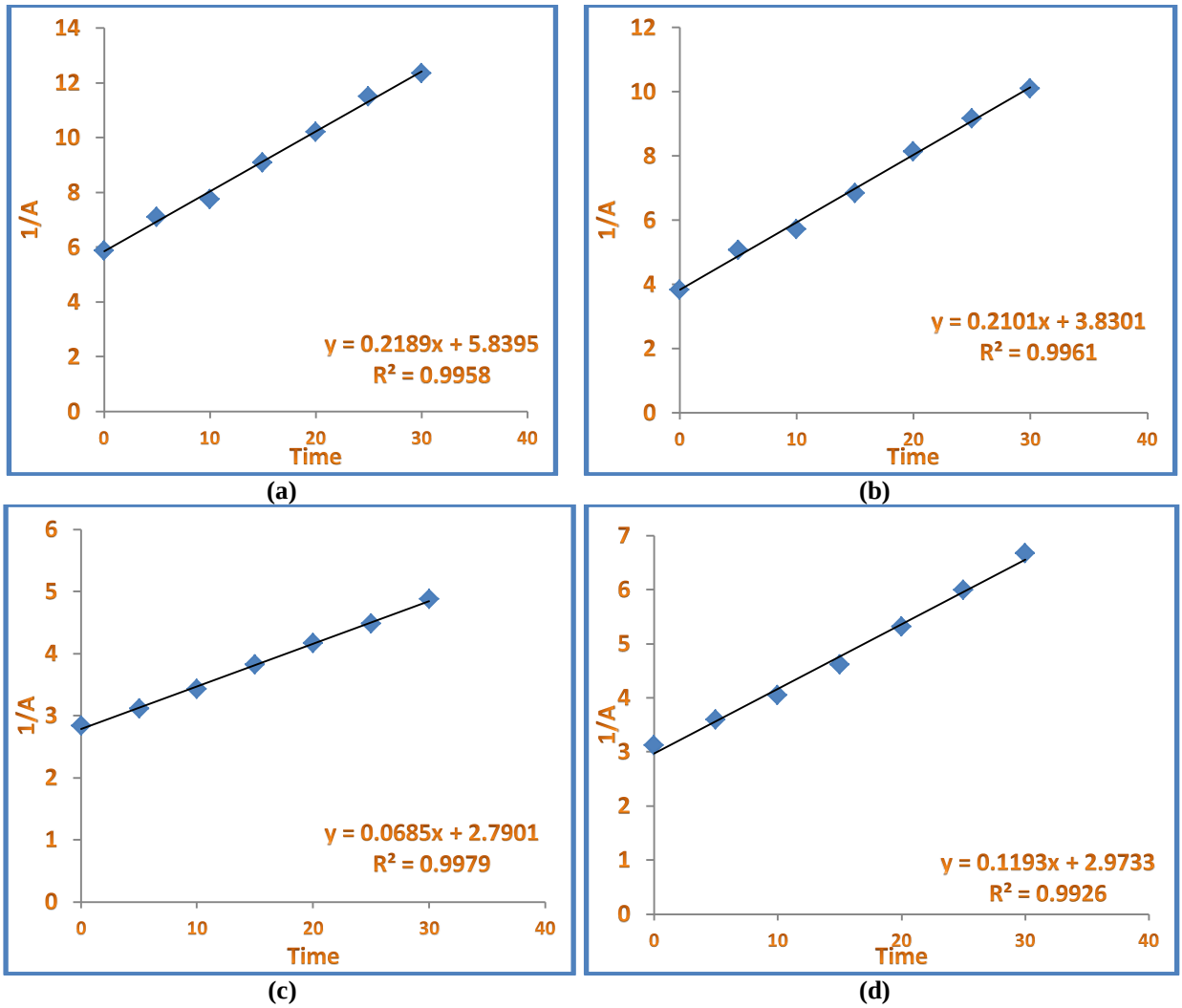


Figure 6-The application of the second order reaction equation for complex of Ni(II)with (a) Glycine (b) Histidine (c) Arginine (d) EDTA.

Table 12- Rate constant of the second order reaction for complex Ni (II) with amino acid.

Complex Title	Second order rate constant k($M^{-1}.min^{-1}$)
Ni(II) + Glycine	$21.8*10^{-2}$
Ni(II) + Histidine	$21*10^{-2}$
Ni(II) + Arginine	$11.9*10^{-2}$
Ni(II) + EDTA	$6.8*10^{-2}$

Conclusion:

The complex of the amino acid(Glycine , Histidine , Arginine , EDTA)with a heavy metal (Nickel(II)) ion shows a high tendency of these amino acid to nickel (II) , this were obvious from the values of their equilibrium constant with the comparison with EDTA which were considered as a good complexing agent used .The thermodynamic parameter shows that this complexation is a spontaneous with an electrostatic interaction and an increase in the order of orientation rate of complexation follows the second order reaction kinetics which were confined by the straight line and a high rate constant.

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