Modern View for Binary and Ternary Complexes of Metal Ions with Amoxicillin and some Amino Acids
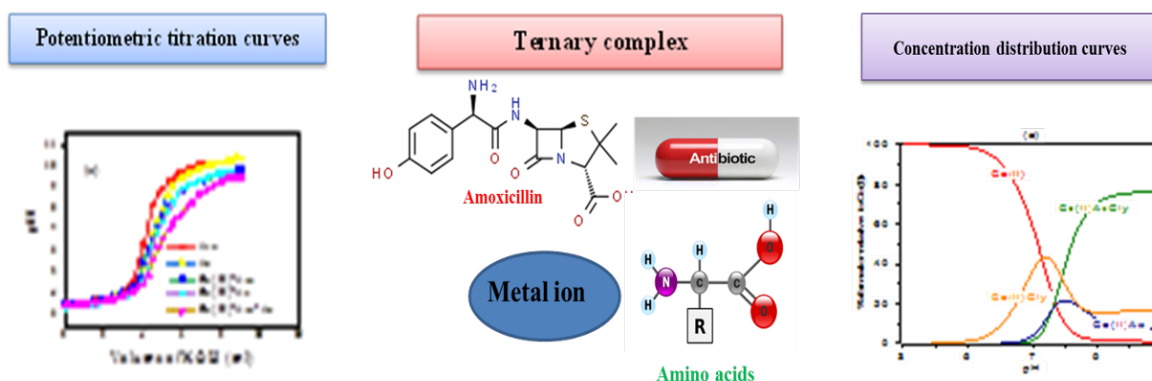
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Graphical Abstract

Abstract

Antibiotics have saved countless lives and continue to be the backbone for treating bacterial infections. β-Lactam antibiotics have been successfully introduced as antibacterial agents in the early 1950s. They are still the most popular drugs for treating bacterial infections of many diseases. As a result, the biological applications of these compounds and their complexes have attracted remarkable attention as they can be used as antibacterial and anticancer agents. From this point, the interactions of metal ions (Cu (II), Co (II), Ni (II), Zn (II), Eu (III), and Tb (III) with amoxicillin(H_2Ax) (Ax) and some selected amino acids (L-glycine (Gly), L-methionine (Met), L-asparagine (Asn), L-histidine (His) and DL-alanine (Ala) have been investigated potentiometrically, 0.1M KNO_3 ionic strength, in an aqueous medium at 20°C. The dissociation constants and formation constants of ligands and their metal complexes were calculated from potentiometric data using the Irriving-Rossotti method. The acid-base characteristics of ligands have been examined and discussed. It was found that complexes formed were of (1100) and (1110) type. The mechanism of ternary complexes formed is association manner. It has been found that amoxicillin does as a primary ligand for the interaction of metal ions in the presence of glycine, alanine, or histidine amino acids. On the other hand, in the case of methionine or asparagine, amoxicillin acts as a secondary ligand. Stabilities of ternary complexes to metal ions were in the following order: Zn(II)< Cu(II) > Ni(II) >Co(II) for transition metal ions and Eu(III) > Tb(III) for lanthanide metal ions. The concentration distribution curves of the binary and ternary complexes formed in the solution were evaluated as a function of pH using the HYSS program.

Keywords: Amoxicillin, amino acids, binary complexes, ternary complexes, potentiometry, stability constant, distribution curves

1. Introduction

During the past decades, the use of metal complexes as pharmaceuticals has gained significant interest due to their therapeutic applications [1]. The transition metal complexes with nitrogen and oxygen donor ligands have multi applications such as anticancer, anti-tubercular, antibiotic, antimicrobial, and antifungal agents [2, 3]. The interaction of metal ions with ligands to form more potent complexes has a significant interest in coordination chemistry. Lanthanide complexes are used in cancer detection and treatment due to the magnetic and chemical characteristics of the lanthanide-ion (Ln(III)). Tri-positive lanthanides are characterized by high charge to volumes ratios, which enable the Ln(III) to form adenovirus complexes, and so various Ln(III) compounds were studied in vivo and in vitro regarding their potential for improving the transduction effectiveness for adenovirus vectors [4]. Lanthanides have just been widely employed as bioimaging agents in the detection of cancer. Amino acids are necessary for biological bodies, and the complexation behavior of transition metal ions with amino acids and peptides has significant biological importance [5, 6].

Ternary complexes serve important roles in biological processes by storing and transporting active substances across cell membranes. These phenomena are strongly related to the formation of higher-order complexes. Therefore, the stability of complexes has major importance as it can affect complexes' biological and chemical activity [7, 8].

In recent years, the chemistry of β-lactam antibiotics about their bioactivities has been of considerable interest [9–11]. The antimicrobial activity of aminopenicillin drug and its metal complexes has been discussed in several literatures [12, 13]. Studies performed on the aminopenicillin drug, and its metal complexes have much physiological and pharmacological importance because the metal complexes of the drug are more potent than the drugs themselves [14].

Amoxicillin (H$_2$Ax, 6-(2-amino-2-(4-hydroxyphenyl) acetamido)-3,3dimetyl-7-oxo-4-
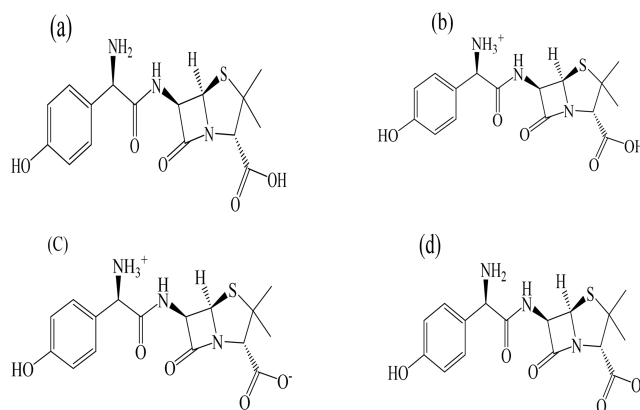

Figure 1: Structures of Amoxicillin at different pH (a)Amoxicillin at solid state (H$_2$Ax), (b) Amoxicillin at pH< 3 (H$_3$Ax$^+$),(c) Amoxicillin at pH 3-7.5 (H$_2$Ax$^\pm$), (d) Amoxicillin atpH 7.5-10 (HAx$^-$)

thia-1-azabicyclo[3,2,0] [2, 3]heptane-2-carboxylic acid) is a very effective penicillin antibiotic that is gaining popularity [15]. It may be found in an aqueous medium as a cation (H$_3$Ax$^+$, pH < 3), zwitterion (H$_2$Ax$^\pm$, pH 3−7.5), or anion (HAx$^-$, pH 7.5-10) [15], [16] as shown in **figure (1)**. Amoxicillin is quite similar to dipeptides in chemical structure and may form stable complexes with metal ions due to their acid-base characteristics.

Amoxicillin is a bactericidal agent acting against susceptible microorganisms by inhibiting cell wall biosynthesis during bacterial multiplication [17, 18]. In both aqueous and methanolic solutions, amoxicillin may make complexes with metal ions [19, 20]. Amoxicillin's coordination molecules, like those of other penicillins, are still understudied by bioinorganic chemists [16], so it was interesting to study the interaction of amoxicillin as a ligand with some metal ions(which have high biological activity) in an aqueous solution.

Research on amoxicillin complexes might be a critical step in developing new treatments to combat antibiotic resistance. Thus, the aim of the present work was the study of the interaction of metal ions (Cu(II), Co(II), Ni(II), Zn(II), Eu(III), and Tb(III)) with amoxicillin(Ax) and some selected amino acids potentiometrically at 20 ^{o}C and ionic strength 0.1M KNO$_3$ in the aqueous medium. The dissociation constants and forma-

tion constants of ligands and their metal complexes were calculated from potentiometric data using the Irriving-Rossotti method [21].

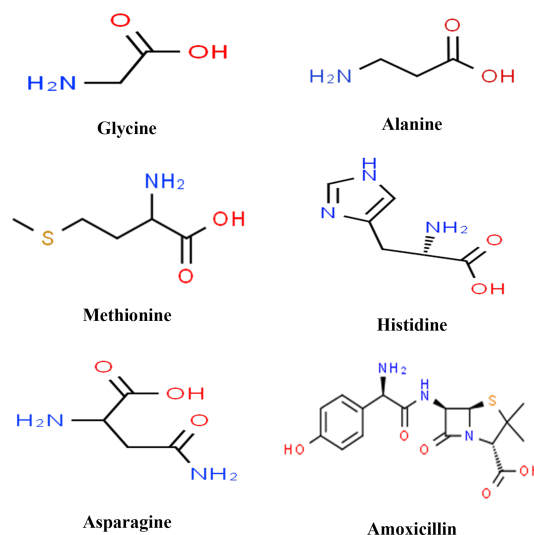## 2. Experimental

2.1. Materials

All compounds used were analytical-grade reagents that were not purified further. Amoxicillin (Ax) and amino acids (L-glycine (Gly), L-methionine (Met), L-asparagine (Asn), L-histidine (His), and DL-alanine (Ala)) were obtained from the Sigma Chemical Company. The chemical structures of amino acids under study were shown in **scheme (1)**. Potassium hydroxide (KOH) was prepared and standardized against a potassium hydrogen phthalate solution (Merck AG). Nitric acid solution was prepared and titrated against standardized potassium hydroxide solution. Metal salts used in this work were: $CuCl_2 \cdot 2H_2O$, $EuCl_3.6H_2O$, $TbCl_3.6H_2O$, $NiCl_2.6H_2O$, $Zn(NO_3)_2.6H2O$, and $Co(NO_3)_2.6H_2O$. Stock solutions of metals were standardized complex-metrically by ethylene-diamine tetra acetic acid disodium salt (EDTA) titrations. The ionic strength was adjusted by using a solution of 0.1M KNO_3. Doubly distilled water was used for the preparation of all solutions.

2.2. Apparatus

Potentiometric pH data were obtained using a commercial Fisher electrode model 825 MP at 20.00 ± 0.100 ^{0}C. The pH-meter has been standardized daily using buffer solutions of pH 4.01 and pH 9.20. Fisher Scientific Circular model 9000 water thermostat has been used to adjust the temperature, and it has been held around 0.1°C of ideal. A magnetic stirrer was used to efficiently stir the solution.

2.3. Procedure

The following are the scheme used for constructing the calibration curves in order to calculating the dissociation constants of ligands and stability constants of binary and tertiary complexes as the following:

Scheme 1: Chemical structures of Amino Acids and Antibiotic

A- HNO_3 ($4x10^{-4}$ M) + KNO_3 (0.1M) solution.

B- Solution a + AA (1×10^{-4}M) (free amino acids).

C- Solution a + Ax (1×10^{-4} M) solution (free amoxicillin).

D- Solution b + Metal ion (1×10^{-4} M), binary system (metal-amino acids).

E- Solution c + Metal ion (1×10^{-4}M), binary system (metal-amoxicillin).

F- Solution a + AA (1×10^{-4} M) + Metal ion (1×10^{-4} M) + Ax (1×10^{-4} M), ternary system.

The total volume of the titrant has been kept being 25.00 ml. A constant ionic strength has been adjusted to be 0.10 M using KNO_3. For all titrations, the concentration of HNO_3 has been adjusted to be 4.00 $x10^{-4}$ M at the beginning of titration in order to fully protonated the ligands.

Table 1: **Dissociation constants of the ligands at I = 0.1 M KNO_3 and 20 °C.**
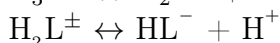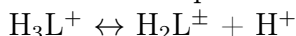
Ligand	pKa$_1$	pKa$_2$
Alanine	——	9.50
Asparagine	——	8.82
Histidine	6.14	10.37
Methionine	——	9.39
Glycine	——	9.49
Amoxicillin	7.16	9.74

3. Result and discussion

3.1. Dissociation constants of ligands:

Amoxicillin contains three sites that may reversibly dissociate a proton to form a negative-charged anion. Amoxicillin may discharge one proton from the carboxylic group, one from the amine group pKa(7.16), and one from phenol group pKa(9.76). The values of the dissociation constants for Amino acids and Amoxicillin are listed in (table 1). In L-Histidine, two dissociation constants of $pKa_1= 6.14$ and $pKa_2= 10.37$ were obtained, which are associated with dissociation of imidazole nitrogen and the amino group of the ligand, respectively. L-glycine, DL-alanine, L-methionine, and L-asparagine dissociated protons from amino groups pKa= 9.49, 9.50, 9.36, and 8.82, respectively. The ionization steps (a) and (b) are as follow:

Ionization steps of amoxicillin and L-histidine
$$H_3L^+ \leftrightarrow H_2L^\pm + H^+$$
$$H_2L^\pm \leftrightarrow HL^- + H^+$$
$$HL^- \leftrightarrow L^- + H^+$$
Ionization steps of alpha-amino acids
$$H_2L^+ \leftrightarrow HL^\pm + H^+$$
$$HL^\pm \leftrightarrow L^- + H^+$$

The first dissociation constant for the Ligands is very low (<2.5) and dissociates in strongly acidic solutions. Therefore, these values could not be measured and obtained through the calculations.

3.2. Binary Complex Formation Equilibria

Amoxicillin and amino acids were titrated in the absence and presence of metal ions. It was observed that titration curves of the metalcomplexes were lower than those of the free ligands curves (**figures 2–6**), indicating that complex formation is associated with the release of the proton (H^+). Formation constants were calculated using the Iriving-Rossotti method and were presented in **table 2**. From the titration curves, $\bar{n}$ (the average number of ligand molecules attached per metal ion) and pL (the free ligand exponent) values have been calculated. It has been found that

the value of (n) was changed from 0.1 to 1.0, indicating that complexes formed in solution are of type (1100). The following equations can represent the formation of binary complexes:
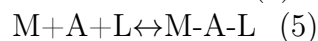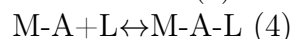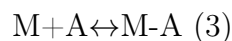$$M+ H_2L^+ \leftrightarrow ML + 2H^+ \quad (1)$$
Or
$$M+ H_3L^+ \leftrightarrow ML + 3H^+ \quad (2)$$

3.3. Ternary Complex Formation Equilibria

It is well known that when a solution contains two different ligands with a metal ion, they may exist in equilibrium either that (i) both the ligands ligate to the metal ion simultaneously (Association mechanism) (eq:5) or (ii) the two ligands may ligate one by one at different pH (Stepwise mechanism) (eq:3,4). The formation constants of ternary complexes have been determined from the potentiometric titration curves.
$$M+A \leftrightarrow M\text{-}A \quad (3)$$
$$M\text{-}A+L \leftrightarrow M\text{-}A\text{-}L \quad (4)$$
$$M+A+L \leftrightarrow M\text{-}A\text{-}L \quad (5)$$

Where A is the primary ligand, L is the secondary ligand, and M is a metal ion.

Log $K^{M(Ax)}_{M(Ax)(AA)}$ and log $K^{M(AA)}_{M(Ax)(AA)}$ constants were calculated for each mixed ligand system. They were compared to each other to decide which ligand acts as a primary ligand and which one acts as a secondary ligand [22].

$$\log K^{M(Ax)}_{M(Ax)(AA)} = \log K^{M}_{M(Ax)(AA)} - \log K^{M}_{M(Ax)} \quad (6)$$

$$\log K^{M(AA)}_{M(Ax)(AA)} = \log K^{M}_{M(Ax)(AA)} - \log K^{M}_{M(AA)} \quad (7)$$

It was found from **tables (3-7)** that Amoxicillin acted as a secondary ligand in ternary complexes involving methionine and asparagine while acting as primary ligands in ternary complexes involving glycine alanine and histidine. DL-alanine ternary complexes' stability was lower than those of glycine complexes, and this isn't due to their basicities because the two amino acids have similar pKa_2 values. Instead, it may be due to steric hindrance caused by the methyl group present on the carbon bearing the amino group. Stabilities of the ternary complexes containing asparagine were lower than those of other amino acids, related to the low basicity of the asparagine-free conjugate
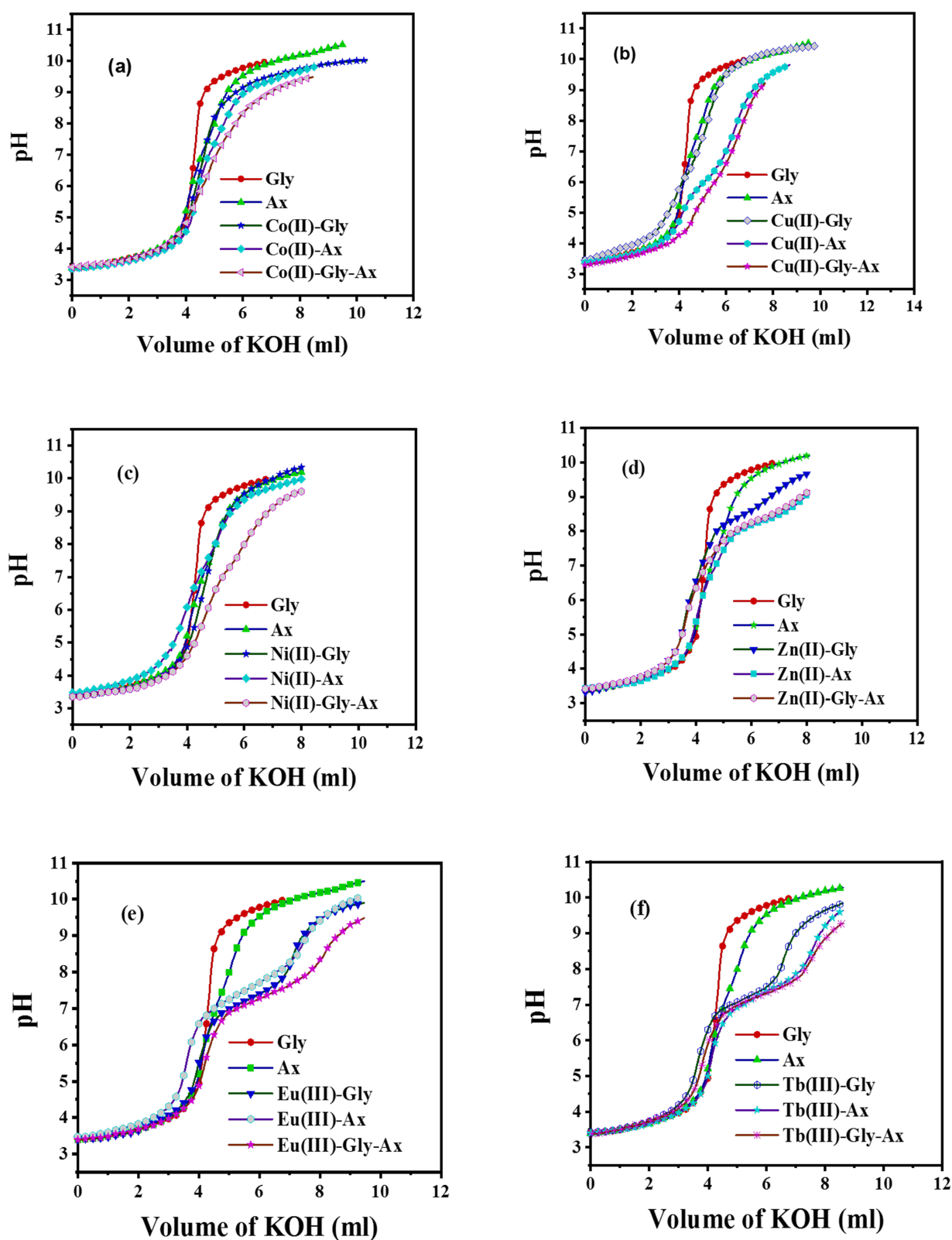
Figure 2: Potentiometric titration curves at I =0.1 M KNO₃ and 20ºC,for: (a) Co(II)– Amoxicillin– Glycine, (b) Cu(II)–Amoxicillin– Glycine,(c) Ni(II)–Amoxicillin– Glycine, (d) Zn(II)– Amoxicillin– Glycine,(e) Eu(III)–Amoxicillin– Glycine and (f) Tb(III)– Amoxicillin– Glycine.
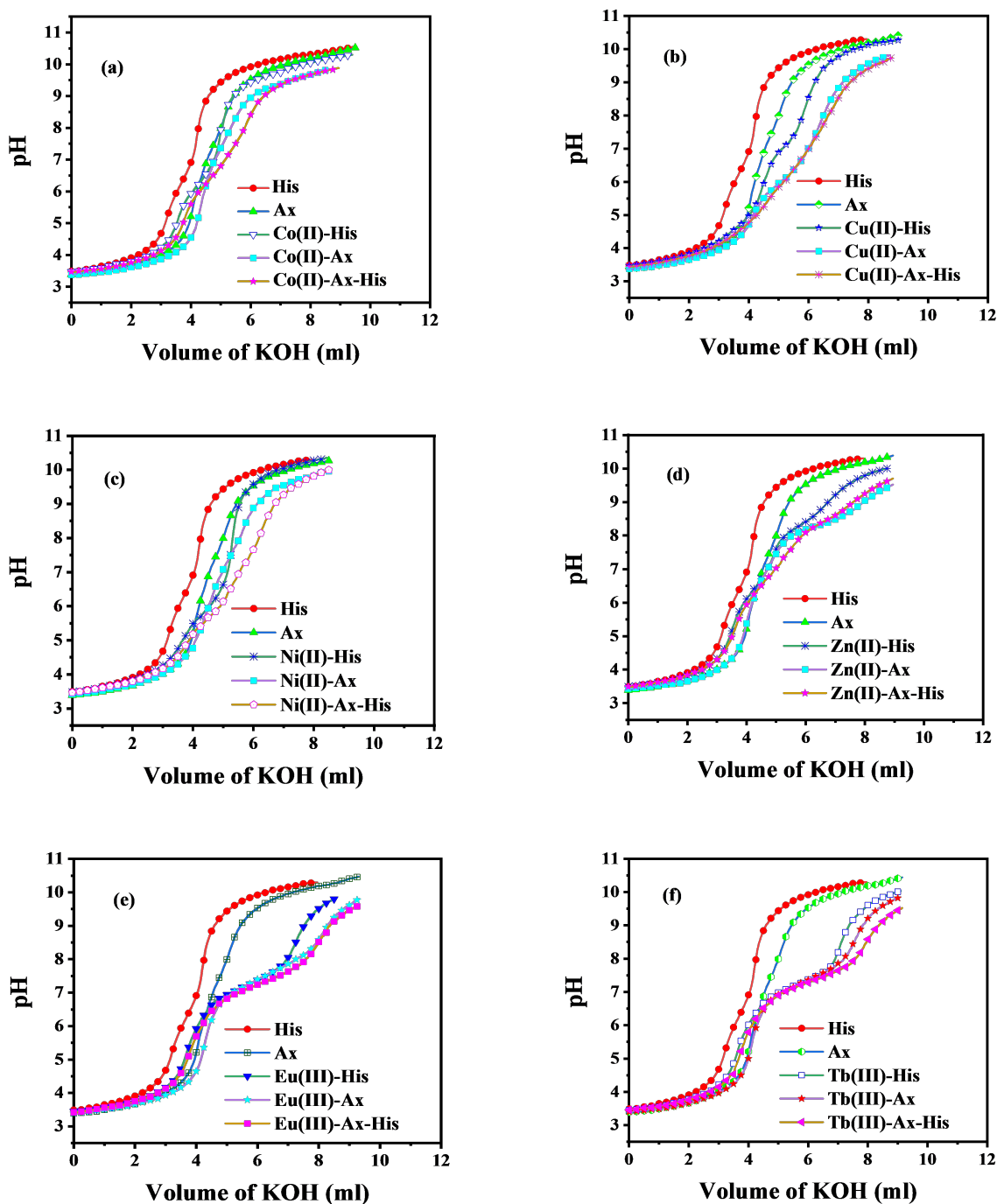
Figure 3: Potentiometric titration curves at $I = 0.1$ M KNO_3 and 20^oC, for: (a) Co(II)–Amoxicillin– Histidine, (b) Cu(II)– Amoxicillin– Histidine,(c) Ni(II)–Amoxicillin–Histidine,(d) Zn(II)–Amoxicillin–Histidine, (e) Eu(III)-Amoxicillin–Histidine and (f) Tb(III)–Amoxicillin– Histidine.
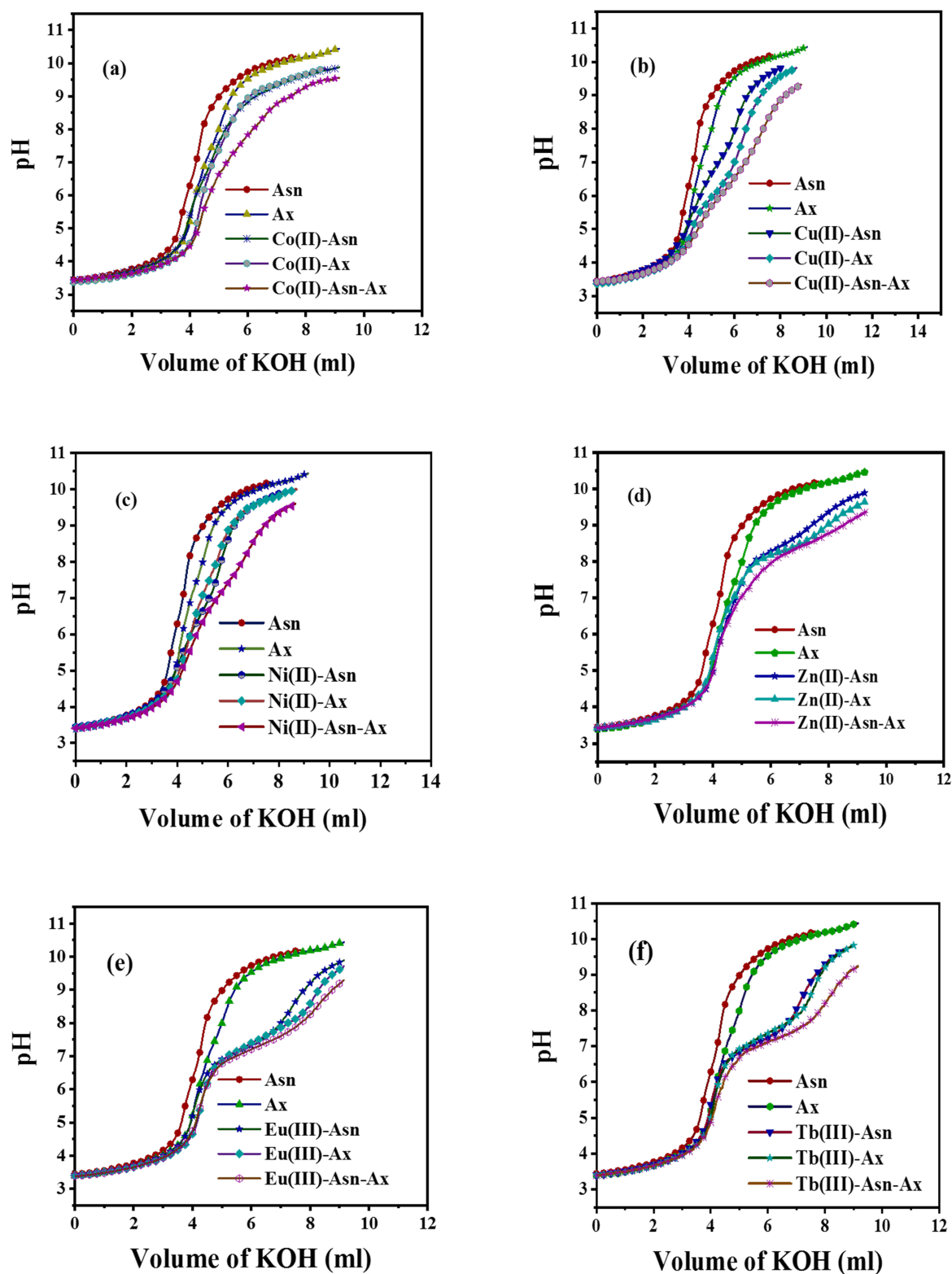
Figure 4: Potentiometric titration curves at I = 0.1 M KNO$_3$ and 20 ^{o}C, for: (a) Co(II)–Asparagine– Amoxicillin, (b) Cu(II)– Asparagine– Amoxicillin,(c) Ni(II)–Asparagine– Amoxicillin, (d) Zn(II)– Asparagine– Amoxicillin,(e) Eu(III)–Asparagine– Amoxicillin and (f) Tb(III)– Asparagine– Amoxicillin.

Figure 5: Potentiometric titration curves at I = 0.1 M KNO$_3$ and 20 ^{o}C, for: (a) Co(II)–Methionine Amoxicillin, (b) Cu(II)– Methionine– Amoxicillin,(c) Ni(II)–Methionine– Amoxicillin, (d) Zn(II)– Methionine– Amoxicillin,(e) Eu(III)–Methionine– Amoxicillin and (f) Tb(III)– Methionine– Amoxicillin.
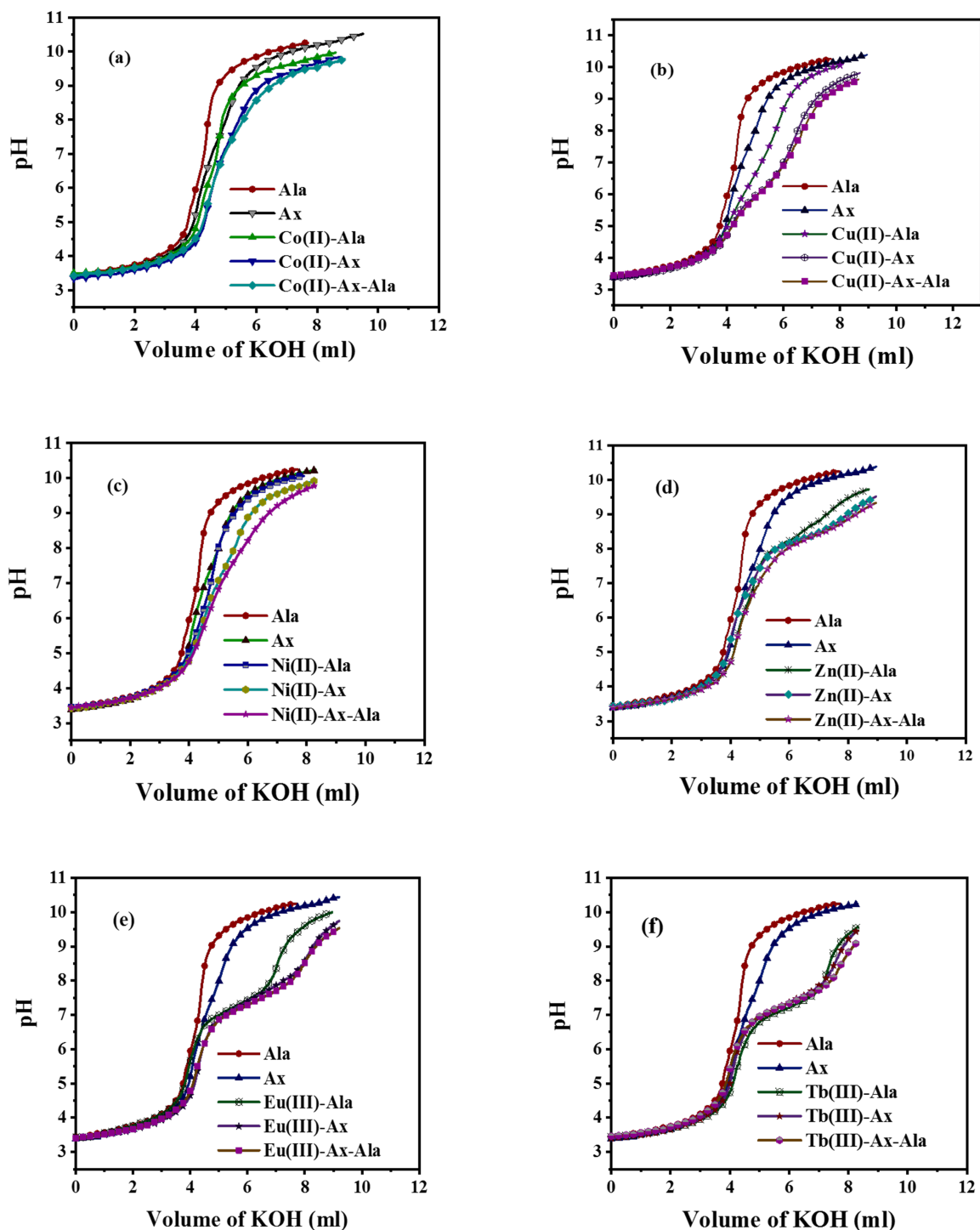
Figure 6: Potentiometric titration curves at I = 0.1 M KNO$_3$ and 20 ^{o}C, for: (a) Co(II) -Amoxicillin–Alanine,(b) Cu(II)–Amoxicillin– Alanine, (c) Ni(II)–Amoxicillin– Alanine,(d) Zn(II)–Amoxicillin–Alanine,(e) Eu(III)–Amoxicillin– Alanine and (f) Tb(III)– Amoxicillin– Alanine.

Table 2: Formation constants for the binary complexes of Metal Ions (M) + Amino acids and Amoxicillin at I = 0.1 M KNO$_3$ and 20 °C.

	log K					
metal ion	Alanine	Asparagine	Methionine	Histidine	Glycine	Amoxicillin
Cu(II)	8.37	6.70	8.15	12.0	8.50	9.46
Co(II)	7.29	5.96	5.05	9.75	6.55	5.77
Ni(II)	8.00	6.75	6.46	11.0	6.96	6.20
Zn(II)	7.57	6.04	6.76	7.15	7.58	6.16
Eu(III)	7.76	6.34	7.43	8.17	9.80	7.43
Tb(III)	7.26	6.38	7.16	8.10	7.03	7.49

Table 3: Formation constants of ternary M+Ala+Ax systems at I = 0.1 M KNO$_3$ and 20°C.

System	log K $^{M}_{M(Ax)(Ala)}$	log K $^{M(Ala)}_{M(Ax)(Ala)}$	log K $^{M(Ax)}_{M(Ax)(Ala)}$	ΔlogK
Co(II)-Ax-Ala	11.57	4.28	5.80	-1.49
Cu(II)-Ax-Ala	14.68	6.31	5.22	-3.15
Ni(II)-Ax-Ala	11.99	3.99	5.79	-2.21
Zn(II)-Ax-Ala	13.54	5.97	7.38	-0.19
Eu(III)-Ax-Ala	15.10	7.34	7.67	-0.09
Tb(III)-Ax-Ala	15.04	7.78	7.55	0.29

Table 4: Formation constants of ternary M+Gly+Ax systems at I = 0.1 M KNO$_3$ and 20°C.

System	log K $^{M}_{M(Ax)(Gly)}$	log K $^{M(Gly)}_{M(Ax)(Gly)}$	log K $^{M(Ax)}_{M(Ax)(Gly)}$	ΔlogK
Co(II)-Ax-Gly	12.10	5.55	6.33	-0.22
Cu(II)-Ax-Gly	14.94	6.44	5.48	-3.02
Ni(II)-Ax-Gly	12.23	5.27	6.03	-0.93
Zn(II)-Ax-Gly	12.87	5.42	6.88	-0.87
Eu(III)-Ax-Gly	15.12	5.32	7.69	-2.11
Tb(III)-Ax-Gly	15.04	8.01	7.55	0.52

Table 5: Formationconstants of ternary M+His+Ax systems at I = 0.1 M KNO$_3$ and 20°C.

System	log K $^{M}_{M(His)(Ax)}$	log K $^{M(His)}_{M(His)(Ax)}$	log K $^{M(Ax)}_{M(His)(Ax)}$	ΔlogK
Co(II)-Ax-His	13.3	3.55	7.53	-2.22
Cu(II)-Ax-His	16	4.00	6.54	-5.46
Ni(II)-Ax-His	14.33	2.92	7.72	-2.87
Zn(II)-Ax-His	15.18	7.90	8.93	1.87
Eu(III)-Ax-His	17.11	8.94	9.68	1.51
Tb(III)-Ax-His	17.07	8.97	9.58	1.48

Table 6: Formation constants of ternary M+Asn+Ax systemsat 20°C, I = 0.1 M KNO$_3$.

System	log K $^M_{M(Asn)(Ax)}$	log K$^{M(Asn)}_{M(Asn)(Ax)}$	log K$^{M(Ax)}_{M(Asn)(Ax)}$	ΔlogK
Co(II)-Asn- Ax	12.03	6.07	6.26	0.30
Cu(II)- Asn-Ax	13.23	6.53	3.77	-2.93
Ni(II)- Asn-Ax	12.85	6.10	6.65	-0.10
Zn(II)- Asn-Ax	12.36	6.26	6.18	0.16
Eu(III)-Asn-Ax	13.75	7.41	6.32	-0.02
Tb(II)- Asn-Ax	13.72	7.34	6.23	-0.15

Table 7: Formation constants of ternary M+Met+Ax systems at 20 °C, I = 0.1 M KNO

System	log K$^M_{M(Met)(Ax)}$	log K$^{M(Met)}_{M(Met)(Ax)}$	log K$^{M(Ax)}_{M(Met)(Ax)}$	ΔlogK
Co(II)-Met-Ax	11.78	6.73	6.01	0.96
Cu(II)-Met-Ax	14.93	6.78	5.47	-2.68
Ni(II)-Met-Ax	11.9	5.9	6.16	-0.76
Zn(II)-Met-Ax	12.58	5.82	6.46	0.34
Eu(III)-Met-Ax	14.91	7.38	7.38	0.05
Tb(III)-Met-Ax	14.85	7.61	7.28	0.20

base (pKa =8.82). The higher stabilities of histidine complexes showed that histidine interacted with the metal ions through amino and imidazole nitrogen to form a six-membered ring [23], other amino acids ligated through amino and carboxylic groups and formed a five-membered ring. The complex stabilities of the ternary systems to the metal ion were:

a- For transition metal ions: Zn(II)< Cu(II) > Ni(II) >Co(II), which follow the Iriving-Williams series, this order could be attributed to ionization potential and ionic radii of metal ions [24].

b- For lanthanide metal ions: Eu(III) > Tb(III), the formation constant of the Ln(III) complexes decreases slightly with increasing atomic number [25].

The greater stability of Cu(II) complexes could be assigned with Jahn–Teller effect [26]. On the other hand, Zn(II)has d^{10} fully occupied d-orbital has low potency to accept electrons from ligands; hence it has lower stability constant. During the titration, no precipitation occurred, indicating that there is no possibility of hydrolysis of the studied metal ions in the presence of excess lig-

and. This showed that the amino acids tend to form more stable metal complexes in the solution. The ternary complexes' stability was compared with those of the corresponding binary complexes using the ΔlogK values. The values of ΔlogK are determined by Equation (8):

ΔlogK= logK$_{M(AA)(Ax)}$ $-($logK$_{M(AA)}$ + logK$_{M(Ax)}$). (8)

The positive Δ log K value for the complexes indicates that the ternary complexes are more stable than the corresponding binary complexes. In contrast, the negative Δ log K value for the complexes indicates that the ternary complexes are less stable than the corresponding binary complexes (binary complexes are preferred). Negative values can be explained based on the presence of a fewer number of coordination sites on the binary complexes.

The concentration distribution of the various species as a function of pH provides a useful description of metal ion binding in the biological system. In the present work, the concentration of the formed complexes increases with increasing
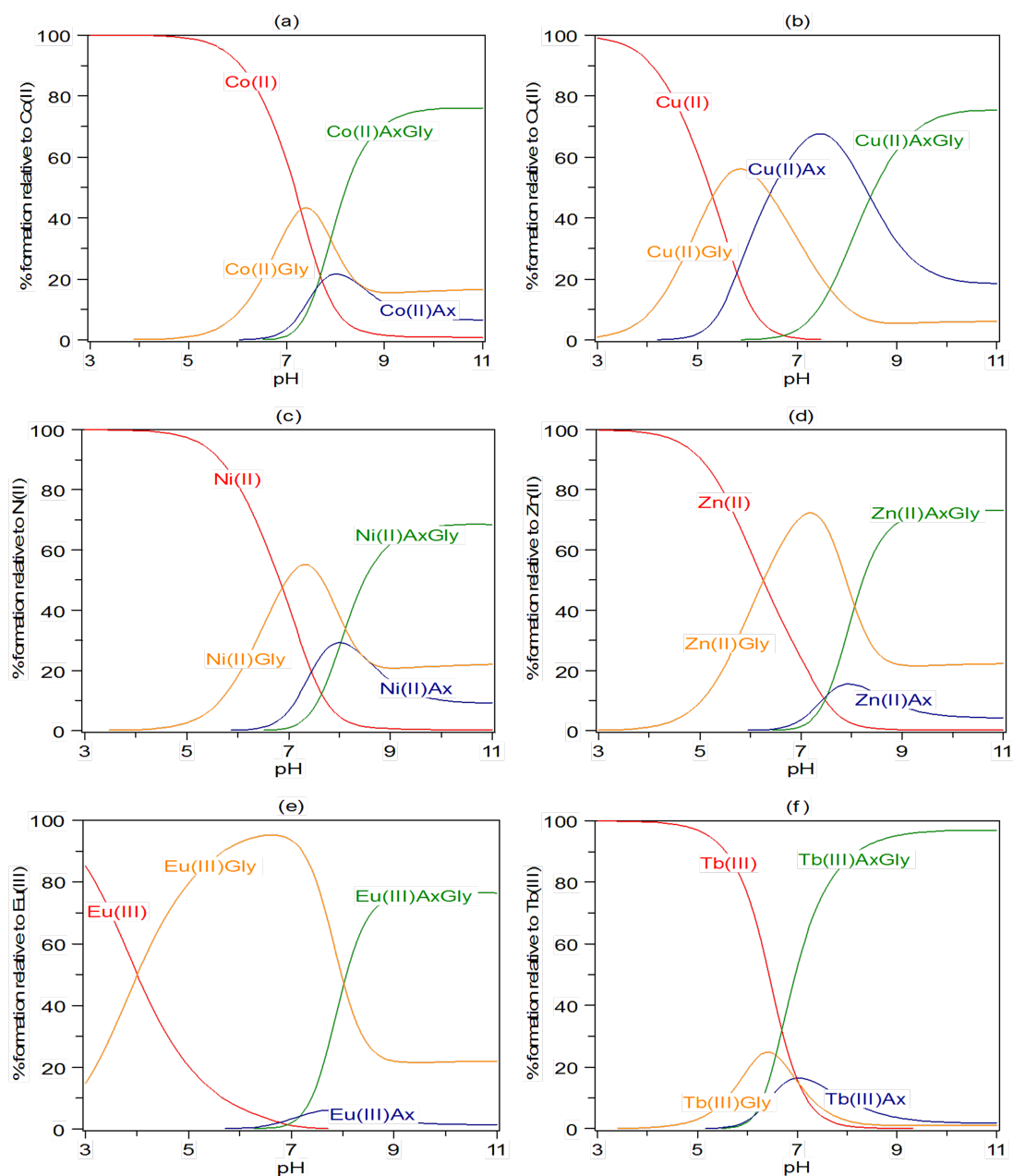
Figure 7: Concentration distribution of various species asa function of pH in : (a) Co(II)-Amoxicillin- Glycine ternary system ,(b)Cu(II)-Amoxicillin- Glycine ternary system,(c) Ni(II)-Amoxicillin- Glycine ternary system, (d) Zn(II)-Amoxicillin- Glycine ternary system, (e)Eu(III)-Amoxicillin- Glycine ternary system, (f) Tb(III)-Amoxicillin-Glycine ternary system
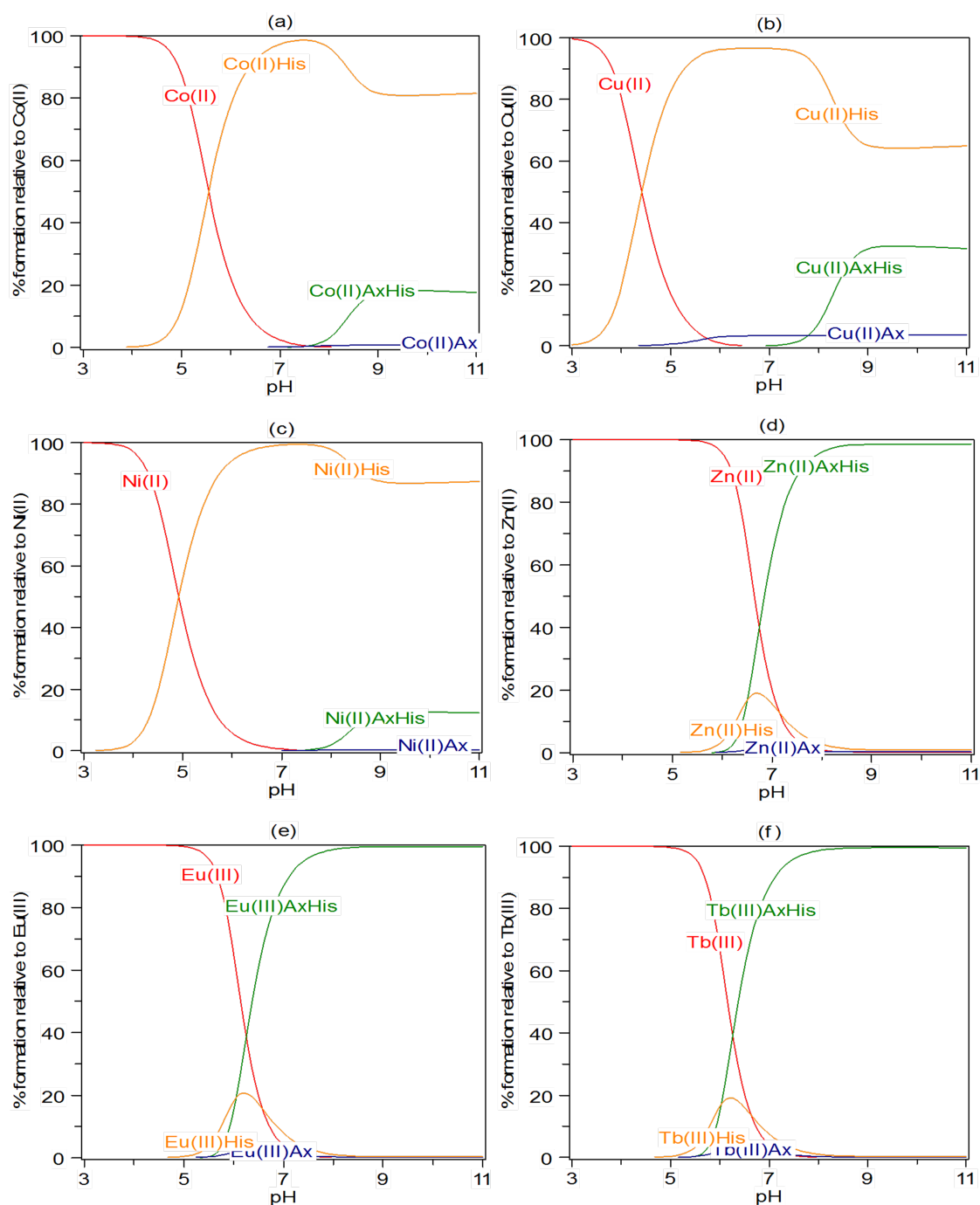
Figure 8: Concentration distribution of various species as a function of pH in : (a) Co(II)-Amoxicillin-Histidine ternary system ,(b) Cu(II) -Amoxicillin-Histidine ternary system,(c) Ni(II)-Amoxicillin-Histidine ternary system, (d)Zn(II)-Amoxicillin -Histidine ternary system, (e) Eu(III)-Amoxicillin-Histidine ternary system, (f) Tb(III) -Amoxicillin-Histidine ternary system .
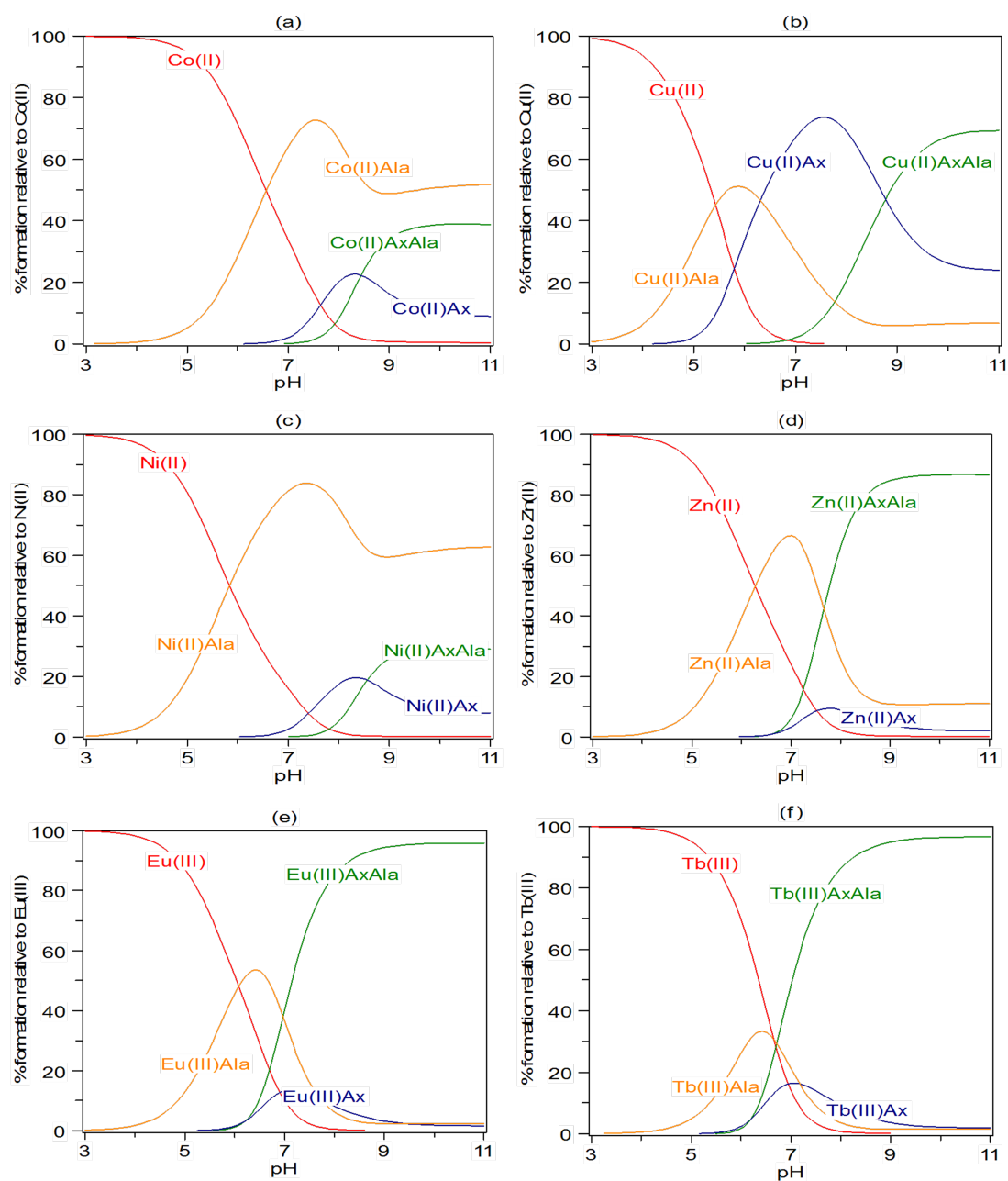
Figure 9: Concentration distribution of various species as a function of pH in : (a) Co(II) -Amoxicillin-Alanine ternary system ,(b)Cu(II)-Amoxicillin-Alanine ternary system,(c) Ni(II)-Amoxicillin-Alanine ternary system, (d) Zn(II)-Amoxicillin-Alanine ternary system, (e) Eu(III)-Amoxicillin-Alanine ternary system, (f) Tb(III)-Amoxicillin-Alanine ternary system
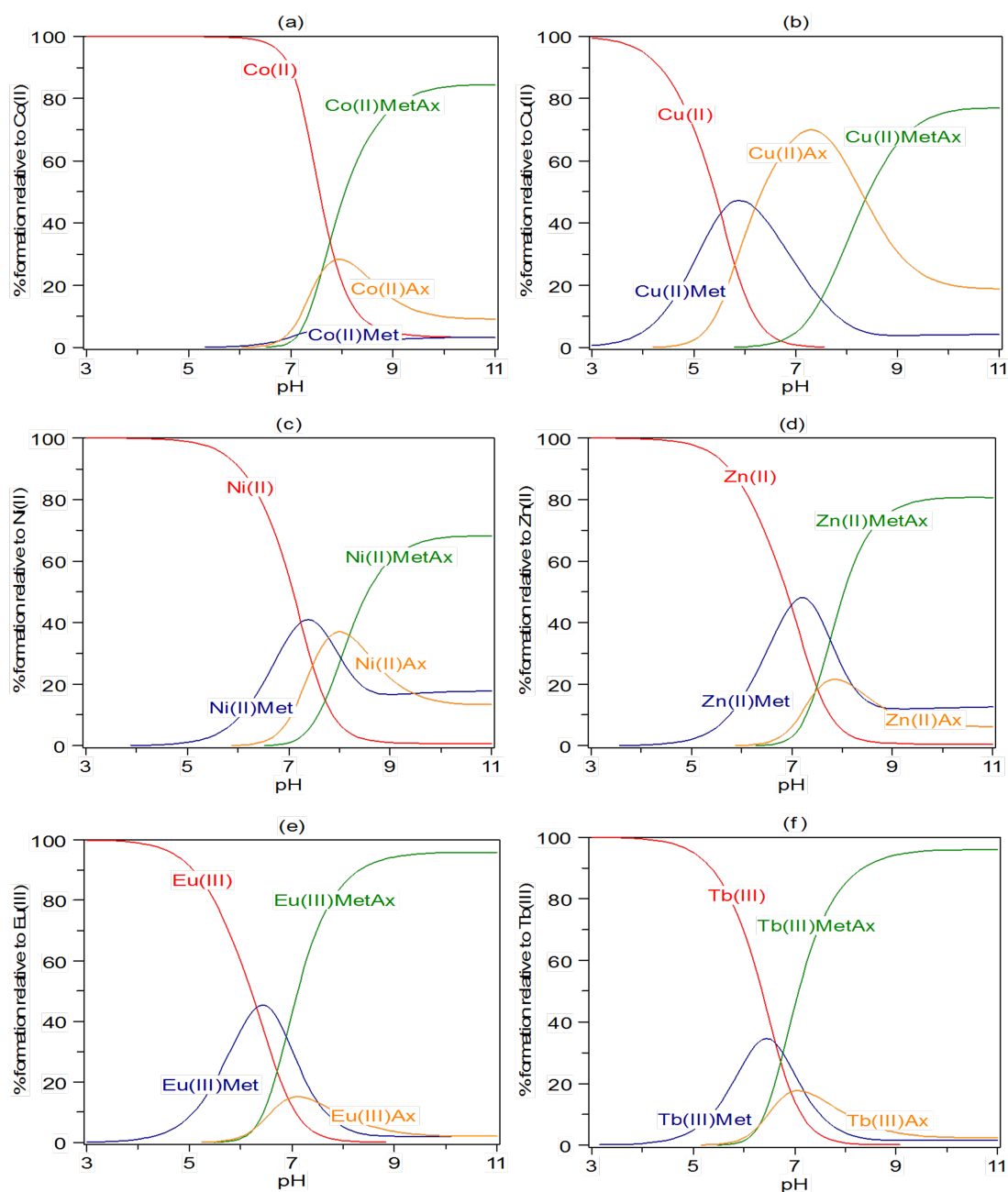.

Figure 10: Concentration distribution of various species asa function of pH in : (a) Co(II)-Methionine-Amoxicillin ternary system ,(b) Cu(II)-Methionine-Amoxicillin ternary system,(c) Ni(II)- Methionine-Amoxicillin ternary system, (d) Zn(II)-Methionine-Amoxicillin ternary system, (e) Eu(III)- Methionine-Amoxicillin ternary system, (f) Tb(III)-Methionine -Amoxicillin ternary system
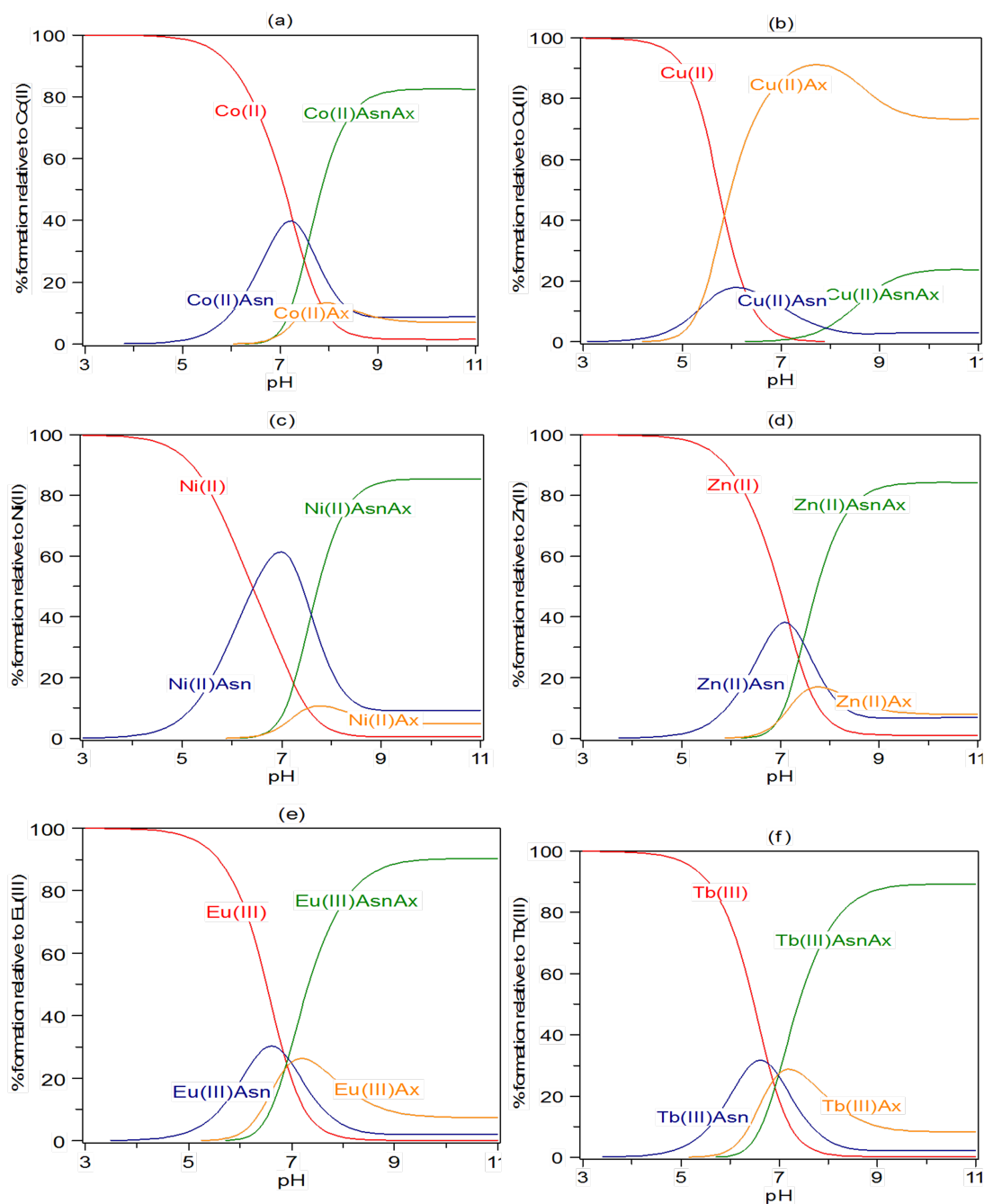
Figure 11: Concentration distribution of various species as a function of pH in : (a) Co(II)-Asparagine-Amoxicillin ternary system ,(b) Cu(II)-Asparagine -Amoxicillin ternary system,(c) Ni(II)- Asparagine -Amoxicillin ternary system, (d) Zn(II)- Asparagine -Amoxicillin ternary system, (e) Eu(III)-Asparagine -Amoxicillin ternary system, (f) Tb(III)-Asparagine -Amoxicillin ternary system

pH, making the formation of complexes more favored in the physiological pH range. Distribution curves of all the binary and ternary systems of Cu(II), Co(II), Ni(II), Zn(II), Eu(III), and Tb(III) were drawn by the HYSS computer program and are given in **Figures(7–11)**. In **figure(7):** metal ions were 100% at the beginning, as reaction proceeded and pH increased, its concentration decreased and binary complexes started to form and had grown until reached maximum values (50% at pH 5.9),(70%,pH 7.5),(80%,pH 7.5),(70%,pH 7), (70%,pH 6.5) and (30%, pH 6.5) for (Cu(II), Co(II), Ni(II), Zn(II), Eu(III) and Tb(III)-Ala binary systems respec tively, while binary systems of amoxicillin reached maximum values (70%, pH 7.7), (20%,pH 8.2), (20%, pH 8.5), (10%,pH 8), (25%,pH 7.5) and (15%,pH 7.1) for (Cu(II), Co(II), Ni(II), Zn(II), Eu(III) and Tb(III) respectively. As pH increased more, concentrations of binary complexes decreased as they dissociated to form ternary complexes. Ternary complexes began to form at pH 7.1, 7, 7.9, 7.0, 6.3 and reached maximum values (70%, pH 10), (39%, pH 9.9), (30%, pH 9.5), (80%, pH 9.5), (90%, pH 9) and (95%, pH 10) for (Cu(II), Co(II), Ni(II), Zn(II), Eu(III) and Tb(III)-Ala-Ax complexes respectively.

4. Conclusion

Ternary complexes of amoxicillin with amino acids and metal ions were studied potentiometrically to determine their stability constants which could provide information about the ability of ligands to form complexes and the activities of the formed complexes, used for biological applications. Ternary complexes were formed in association manner. Stability constants were found to follow the order Zn(II)< Cu(II) > Ni(II) >Co(II) for transition metal ions and Eu(III) > Tb(III) for lanthanide metal ions. In the present paper, some ternary complexes are more stable than the corresponding binary complexes. The concentration distribution diagrams of all species formed in solution were investigated and discussed.

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