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Equilibrium Studies of Schiff Bases and Their Complexes with Ni(II), Cu(II) and Zn(II) derived from Salicylaldehyde and Some α-Amino Acids

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The acid-base equilibria of Schiff bases derived from salicylaldehyde, glycine, alanine, serine, tyrosine, and phenylalanine, and their Ni(II), Cu(II) and Zn(II) complex formation equilibria were investigated by a potentiometric method in aqueous solution ($t = 25°C, \mu = 0.1\,M$, KCl). The data from the potentiometric titrations were evaluated by means of the BEST computer program. The order of the formation constant values of the Schiff bases was Sal-Ala > Sal-Gly > Sal-Ser > Sal-Phe > Sal-Tyr, which is the same order as the increasing log K_1 values of amino acids (and the log K_2 values of tyrosine) with the exception of an inversion between serine and phenylalanine. Also, it was seen that the stability constants, log β_1 and log β_2, of Schiff base–metal complexes vary for all the metal ions investigated, *viz*., Sal-Gly > Sal-Ala > Sal-Ser > Sal-Tyr > Sal-Phe with the exception of Sal-Gly in the copper complex. The effect of the nature of the amino acids on their formation, protonation and stability constants was also discussed.

KEY WORDS: Schiff bases; salicylaldehyde; α-amino acid; formation constant; protonation constant; stability constant; potentiometric method.

1. INTRODUCTION

A large number of Schiff bases and their complexes have been studied for their interesting and important properties, *e.g*., their ability to reversibly bind oxygen,[1] their catalytic activity in the hydrogenation of olefins,[2] the transfer of an amino group,[3] their photochromic properties,[4] their complexing ability towards some toxic metals.[5] On the other hand, the interactions between metal ions and amino acids is of considerable interest as models for metal–protein reactions and models in a variety of biological systems.[6] The ternary complexes of the Schiff bases and

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amino acids with metal ions bear the importance of both Schiff bases and amino acids.[7]

Metal ions greatly enhance the formation of pyridoxal-amino acid Schiff bases, which play an important role in many biological processes involving amino acids and keto acids, such as transamination, decarboxylation and deamination in aqueous solution.[8,9] The metal complexes of Schiff bases lend themselves ideally to a study of the effect of metal ions on the equilibrium between two small molecules and a large molecule, which may be produced from them. The chemistry of the metal complexes of amino acid Schiff bases are of interest, because of their possible biological importance.[10–24] Transition metal complexes of salicylaldehyde–amino-acid Schiff bases are nonenzymatic models for pyridoxal-amino acid systems, which are of considerable importance as key intermediates in many metabolic reactions of amino acids catalyzed by enzymes, which require pyridoxal as a cofactor.

Although much work has been reported on the synthesis and structural charactarization of the metal complexes of salicylidene amino acids, a literature survey reveals that the formation and protonation constants of Schiff bases prepared from salicylaldehyde and amino acid, and the stability constants of their complexes with Ni(II), Cu(II) and Zn(II), have not been determined systematically under the conditions studied here. Particilarly, some of the equilibrium constants for salicylidenephenylalanine, salicylideneserine and salicylidenetyrosine, which were investigated in this study, have not been reported previously. This article, therefore, deals with the determination of the stoichiometric formation and protonation constants of salicylideneglycine (Sal-Gly^{2-}), salicylidenealanine (Sal-Ala^{2-}), salicylidenephenylalanine (Sal-Phe^{2-}), salicylideneserine (Sal-Ser^{2-}) and salicylidenetyrosine (Sal-Tyr^{2-}), and the stability constants of their complexes with Ni(II), Cu(II) and Zn(II) in aqueous medium. Also, in this study, the stoichiometric protonation constants of saliyclaldehyde (Sal), glycine (Gly), L-alanine (Ala), L-phenylalanine (Phe), L-serine (Ser) and L-tyrosine (Tyr), and the stability constants of their complexes with Ni(II), Cu(II) and Zn(II) have been reported, and the relationship between the stoichiometric protonation constants of the amino acids and the formation constants of salicylideneamino acids has been investigated.

The stoichiometric equilibrium constants were measured by a potentiometric titration method at $(25.0 \pm 0.1)\,^{\circ}C$ under a nitrogen atmosphere in aqueous solutions, in which the ionic strength was adjusted with 0.10 *M* KCl and calculations were carried out using the BEST computer software.[25,26]

2. EXPERIMENTAL

Salicylaldehyde, α-amino acids and the other reagents were purchased from Merck and used as received. Stock solutions (0.030 *M*) were prepared in water and their purities were checked by potentiometric titration.[27,28] A 0.1 *M* HCl solution was prepared in water and standardized by titration against primary

standard sodium carbonate. Double-distilled deionized water was used throughout the experiments. Chemically pure KCl was used to maintain a constant ionic strength. Alkali solutions containing 0.10 *M* KCl were prepared using KOH and standardized potentiometrically against an HCl solution using Gran plot techniques and also allowing a determination of the dissolved carbonate impurity.[29,30] Stock solutions of Ni(II), Zn(II) and Cu(II) ions were prepared by dissolving the required quantities of the respective chloride compound in water containing the calculated quantity of hydrochloric acid to prevent hydrolysis. This solution was standardized by both the atomic absorption spectroscopic method and titration with EDTA.[31]

Potentiometric titrations were performed in a 65 mL glass vessel equipped with a combined pH electrode (Ingold), nitrogen inlet and outlet tubes, a magnetic stirrer, and titrant inlet. The electrode was modified by substituting its aqueous potassium chloride solution for a mixture of 0.10 *M* KCl saturated with AgCl. An Orion Model 940A pH Ionmeter was used to measure the cell e.m.f. (the uncertainity of the e.m.f. measurements was ±0.1 mV). The KOH solution was added with an Orion 960 automatic Titermeter. The temperature was maintained at (25.0 ± 0.1) °C.

The potentiometric cell was calibrated before each experiment to obtain pH (= $-\log [H^+]$) values for the titration medium.[25] The potentiometric titrations were carried out at constant temperature and in an inert atmoshere of nitrogen with CO_2-free standardized 0.10 *M* KOH in a 50.0 mL solution containing 0.10 *M* KCl: (i) (2.5×10^{-3}) *M* HCl (for cell calibration); (ii) (1.5×10^{-3}) *M* salicylaldehyde (for protonation constants); (iii) (1.50×10^{-3}) *M* HCl + (1.50×10^{-3}) *M* amino acid (for protonation constants); (iv) (1.50×10^{-3}) *M* HCl + (1.5×10^{-3}) *M* salicylaldehyde + (1.5×10^{-3}) *M* amino acid (for formation and protonation constants of Schiff bases); (v) (1.5×10^{-3}) *M* HCl + (1.5×10^{-3}) *M* salicylaldehyde or amino acid + (5.0×10^{-4}) *M* $NiCl_2$, $CuCl_2$ or $ZnCl_2$ (for stability constants of salicylaldehyde or amino acids with Ni(II), Cu(II) or Zn(II)); and (vi) (1.5×10^{-3}) *M* HCl + (1.5×10^{-3}) *M* salicylaldehyde + (1.5×10^{-3}) *M* amino acids + (7.5×10^{-3}) *M* $NiCl_2$, $CuCl_2$ or $ZnCl_2$ {for stability constants of the Schiff base complexes with Ni(II), Cu(II), or Zn(II)}. The cell potential was read after waiting to establish the equilibrium throughout the titration, which was performed at a constant ionic strength of 0.1 *M* with KCl. The BEST computer software was used to determine the formation, protonation and stability constants from the potentiometric data.[25,26]

3. RESULTS AND DISCUSSION

3.1. Binary Systems

The stoichiometric protonation constants of salicylaldehyde, glycine, alanine, phenylalanine, serine and tyrosine, and the stoichiometric stability constants of these amino acids and the salicylaldehyde complexes with Ni(II), Cu(II) and Zn(II) that were obtained here and elsewhere[32–36] are presented in Table I.

Table I. Stoichometric Protonation of α-Amino Acids and Salicylaldehyde, and the Formation Constants of α-Amino Acids and Salicylaldehyde: M(II) Complexes {Cu(II), Ni(II) and Zn(II)} in Water Media $\{t = (25.0 \pm 0.1)\ ^\circ\text{C}, \mu = 0.1\ \text{mol-L}^{-1}, \text{KCl}\}$

	H^+			Ni^{+2}			Cu^{+2}		Zn^{+2}		
α-amino acids	$\log K_1^H$	$\log K_2^H$	$\log K_3^H$	$\log \beta_1^{Ni}$	$\log \beta_2^{Ni}$	$\log \beta_3^{Ni}$	$\log \beta_1^{Cu}$	$\log \beta_2^{Cu}$	$\log \beta_1^{Zn}$	$\log \beta_2^{Zn}$	$\log \beta_3^{Zn}$
Glycine	9.58 ± 0.01	2.37 ± 0.02	—	5.78 ± 0.01	10.51 ± 0.02	13.83 ± 0.06	8.12 ± 0.02	14.87 ± 0.05	4.93 ± 0.01	9.12 ± 0.03	11.47 ± 0.05
	9.58 ± 0.05^a	2.32 ± 0.07^a	—	5.78 ± 0.05^b	10.58 ± 0.07^b	14 ± 0.2^b	8.18 ± 0.04^b	15.0 ± 0.1^b	4.96 ± 0.03^b	9.19 ± 0.08^b	11.6 ± 0.1^b
	9.52 ± 0.02^c	2.37 ± 0.004^c	—	—	—	—	—	—	—	—	—
l-Alanine	9.74 ± 0.01	2.44 ± 0.01	—	5.41 ± 0.01	9.82 ± 0.03	12.86 ± 0.03	8.14 ± 0.02	14.76 ± 0.04	4.57 ± 0.02	8.61 ± 0.03	10.73 ± 0.01
	9.70 ± 0.02^b	2.31 ± 0.02^b	—	5.40 ± 0.06^b	9.9 ± 0.1^b	12.9 ± 0.1^b	8.15 ± 0.07^c	14.9 ± 0.1^c	4.56 ± 0.06^b	8.55 ± 0.05^b	10.6 ± 0.1^b
	9.67 ± 0.02^c	2.35 ± 0.01^c	—	—	—	—	—	—	—	—	—
l-Serine	9.05 ± 0.01	2.09 ± 0.02	—	5.39 ± 0.01	10.00 ± 0.01	13.40 ± 0.1	7.93 ± 0.02	14.48 ± 0.03	4.66 ± 0.01	8.89 ± 0.08	—
	9.06 ± 0.06^a	2.13 ± 0.04^a	—	5.45 ± 0.03^a	9.96 ± 0.02^a	13.02 ± 0.3^a	7.98 ± 0.03^a	14.48 ± 0.09^a	4.65 ± 0.01^a	8.68 ± 0.3^a	—
l-Phenylalanine	9.11 ± 0.01	2.23 ± 0.03	—	5.13 ± 0.01	9.65 ± 0.03	—	7.85 ± 0.01	14.65 ± 0.02	4.20 ± 0.03	8.30 ± 0.05	—
	9.12 ± 0.02^d	1.89 ± 0.03^d	—	—		—	7.72 ± 0.02^d	14.81 ± 0.03^d	—	—	—
	9.09 ± 0.04^b	2.17 ± 0.05^b	—	—		—	7.81 ± 0.01^e	14.63 ± 0.04^e	—	—	—
l-Tyrosine	10.04 ± 0.01	8.99 ± 0.03	2.17 ± 0.01	$4.99 \pm 0.02^*$	$9.48^* \pm 0.05$	—	$7.80^* \pm 0.01$	$14.91^* \pm 0.02$	$4.16^* \pm 0.01$	$8.23^* \pm 0.03$	—
	10.14 ± 0.1^a	9.04 ± 0.05^a	2.17 ± 0.01^a	5.10 ± 0.08^a	9.46 ± 0.2^a	—	7.81 ± 0.1^a	14.74 ± 0.01^a	4.16 ± 0.01^a	8.27 ± 0.06^a	—
Salycilaldehyde	8.12 ± 0.01	—	—	3.82 ± 0.01	6.41 ± 0.01	—	5.42 ± 0.03	9.78 ± 0.08	2.95 ± 0.01	—	—
	8.13 ± 0.01^b	—	—	3.58^f	6.5^f	—	5.36^f	10.11^f	2.87^f	5.00^f	—

[a] Reference 27 ($\mu = 0.1$; $t = 25^\circ$C).
[b] Reference 29 ($\mu = 0.1$; $t = 25^\circ$C).
[c] Reference 30 ($\mu = 0.12$; $t = 25^\circ$C).
[d] Reference 28 ($\mu = 0.12$; $t = 25^\circ$C).
[e] Reference 31 ($\mu = 0.12$; $t = 25^\circ$C).
[f] Reference 29 ($\mu = 0.5$; $t = 25^\circ$C).

The values of the protonation and stability constants are in reasonable agreement with data available in the literature.

3.2. Ternary Systems

The equilibrium pH profiles were plotted as a function of added base for the systems containing equimolar quantities of amino acids and salicylaldehyde to determine whether the Schiff bases form under the conditions studied. An example plot is given in Fig. 1, where the experimental values labeled as Gly-Sal SB is different from the pH profile calculated assuming that there is no

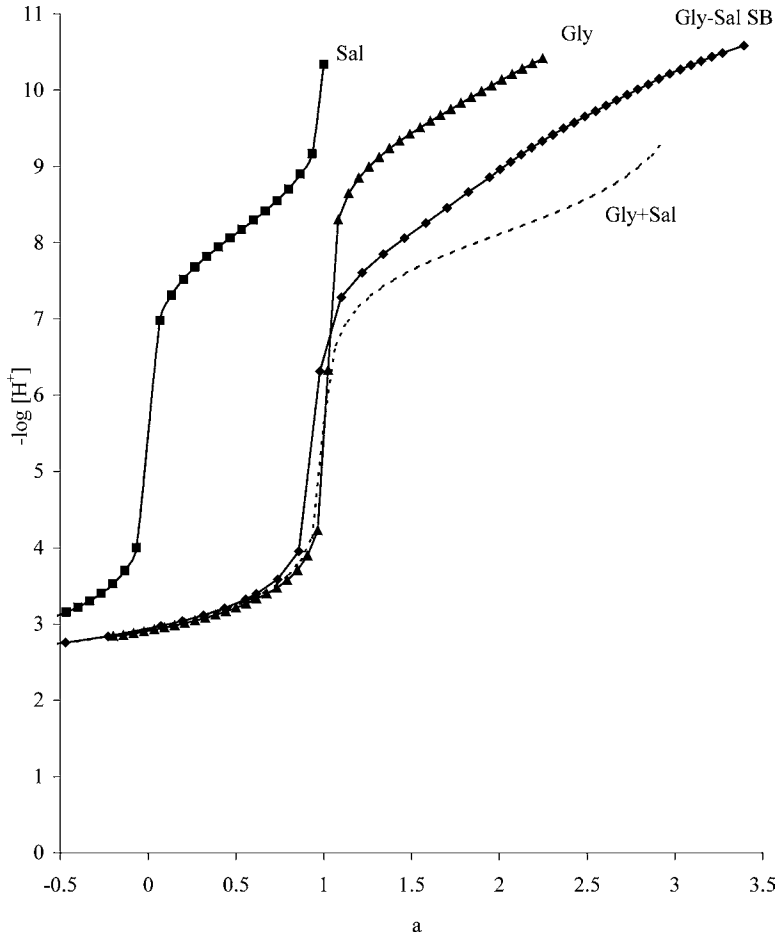


Fig. 1. Potentiometric titration curves of salicylaldehyde, glycine, and salicylideneglycine as a function of added KOH (a = moles of base added per mole of ligand).

interaction between the two Schiff base-forming components, indicated by the dotted curve. Although the differences seem small in the acidic and neutral regions, the computational analysis indicated the formation of a substantial amount of HSB, H_2SB, H_3SB species and relatively smaller amounts of the Schiff bases.

The stoichiometric formation constants ($\log \beta_0$), which were evaluated for the formation of the unprotonated Schiff bases from the unprotonated forms of various amino acids and salicylaldehyde, and the stoichiometric protonation constants of Schiff bases were calculated by using the computer program mentioned above and are listed in Table II together with the stoichiometric stability constants of the Ni(II), Cu(II), and Zn(II) complexes of these Schiff bases where the values are the cumulative constants, β, for the reactions,

$$i\ X^{n+} + j\ Sal^- + j\ AA^- \rightleftharpoons X_i(Sal - AA)_j^{n-2} + H_2O \tag{1}$$

where X is H^+, Ni(II), Cu(II), or Zn(II) and AA^- are amino acids.

An inspection of the $\log \beta_0$ values for the formation of unprotonated Schiff bases (Table II) reveals that the order is Sal-Ala > Sal-Gly> Sal-Ser > Sal-Phe > Sal-Tyr, which is the same order as the increasing $\log K_1$ values of amino acids (and the $\log K_2$ values of tyrosine) with the exception of an inversion between serine and phenylalanine. The inversion of these two amino acids may be explained by steric effects. The steric interference between the phenyl ring in phenylalanine and the planar Sal^- is higher than between the hydroxyl group in serine and the planar Sal^-. The $\log \beta_0$ values for various unprotonated Schiff bases reported[8,13,21] for salicylaldehyde range between 0.14 and 1.34 in agreement with the constants reported here, which are in the range from 0.15 to 0.83.

The $\log K_1$ values of the Schiff bases that can be calculated from the data in Table II using Eq. (2) are 11.13 (Sal-Gly), 10.96 (Sal-Ala), 11.08 (Sal-Ser), 11.77 (Sal-Phe), and 12.15 (Sal-Tyr). The data obtained by Leach and Leussing[21] for (Sal-Gly) and (Sal-Ala) are in good agreement with our finding (see Table II).

$$\log\ K_1 = \log\ \beta_1 - \log\ \beta_0 \tag{2}$$

A comparison between the $\log K_1$ values for Schiff bases and those for $\log K_1$ for amino acids (and the $\log K_2$ values of tyrosine) suggest that the azomethine nitrogen has a higher basicity than those of amino acids from which it is derived, because the proton bound to the azomethine nitrogen is stabilized by the H-bonding interaction with phenoxide and carboxylate groups in all the Schiff bases.[8]

When the $\log K_1$ values for Schiff bases are compared, the following order can be seen.

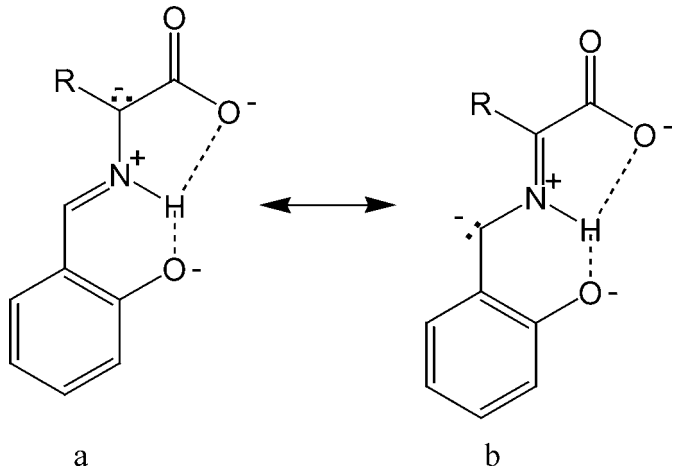
$$Sal - Tyr > Sal - Phe > Sal - Gly > Sal - Ser > Sal - Ala$$

Table II. Formation and Protonation Constants of the Schiff Bases and Stability Constants of the Schiff Base:{Cu(II), Ni(II) and Zn(II)} Complexes in Water Media $\{t = (25.0 \pm 0.1)\,^{\circ}\mathrm{C}, \mu = 0.1\ ^{\circ}\mathrm{mol\text{-}L^{-1}}, \mathrm{KCl}\}$

		H^+				Ni^{+2}		Cu^{+2}	Zn^{+2}	
Schiff bases	$\log \beta_0$	$\log \beta_1^H$	$\log \beta_2^H$	$\log \beta_3^H$	$\log \beta_4^H$	$\log \beta_1^{Ni}$	$\log \beta_2^{Ni}$	$\log \beta_1^{Cu}$	$\log \beta_1^{Zn}$	$\log \beta_2^{Zn}$
Salicylideneglycine	0.55 ± 0.02	11.68 ± 0.01	19.25 ± 0.02	21.68 ± 0.03	—	10.34 ± 0.05	18.7 ± 0.1	16.48 ± 0.01	9.48 ± 0.03	16.6 ± 0.1
	0.48[a]	11.69[a]	—	—	—	10.75[a]	18.89[a]	16.15[a]	9.65[b]	16.73[b]
Salicylidenealanine	0.83 ± 0.03	11.79 ± 0.01	19.21 ± 0.03	21.62 ± 0.03	—	10.10 ± 0.02	18.6 ± 0.2	16.98 ± 0.02	9.05 ± 0.03	15.98 ± 0.2
	0.78[a]	11.75[a]	—	—	—	—	—	—	9.56[b]	16.23[b]
Salicylideneserine	0.40 ± 0.02	11.48 ± 0.02	19.48 ± 0.03	21.63 ± 0.04	—	9.99 ± 0.02	18.4 ± 0.3	16.72 ± 0.03	8.85 ± 0.02	16.0 ± 0.1
Salicylidenephenylalanine	0.16 ± 0.03	11.93 ± 0.02	19.87 ± 0.02	22.10 ± 0.02	—	9.24 ± 0.03	17.3 ± 0.2	16.26 ± 0.03	8.22 ± 0.03	15.2 ± 0.2
Salicylidenetyrosine	0.15 ± 0.03	12.30 ± 0.03	21.66 ± 0.02	29.34 ± 0.02	31.55 ± 0.04	9.26 ± 0.02	17.5 ± 0.1	16.20 ± 0.02	8.27 ± 0.03	15.3 ± 0.3

[a]Reference 14.

[b]Reference 15.



Scheme 1.

This order can be used as an indication to the extent of the contributions of the parent amino acids to the basicity of the azomethine nitrogen. If the log K_1 value of Sal-Ser is neglected it is observed that there is a somewhat negative correlation between the log K_1 values of Schiff bases and the log K_1 values of amino acids (and the log K_2 values of tyrosine) ($r = -0.988$). This negative correlation can be explained by the formation of the carbonion[37] (Scheme I).

The resonance forms a and b of the α-deprotonated Schiff base, which is monoprotonated at the azomethine nitrogen, are stabilized by the covalent N—H bond as well as by delocalization of the negative charge. In contrast to the other Schiff bases, salicylidenephenylalanine and salicylidenetyrosine, because they contain a phenyl ring, which is electron withdrawing due to conjugation, the negative charge is delocalized and the protons, which are bound to the azomethine nitrogen, are stabilized. Also, the conjugation effect reduces the log K_2 value of tyrosine that is related to the phenolate protonation of the phenyl ring.

The other protonation sequence of the Schiff base is assigned as follows: the protonation at the phenolic oxygen and protonation of the carboxylate group. The constant for phenoxide protonation of the salicylidene Schiff bases is smaller than the value observed for phenolate protonation of salicylaldehyde. This low affinity of the phenolate group for a proton arises from the repulsive influence of the nearby imminium ion coupled with the energy required to break the imminium-phenolate hydrogen bond.[8]

Determination of the equilibrium constants permits the calculation of the concentration of all species that are formed in appreciable concentrations as a function of p[H] or other solution conditions. The distribution curve of each Schiff base concentration *vs.* p[H] (Fig. 2) shows that the concentration of the

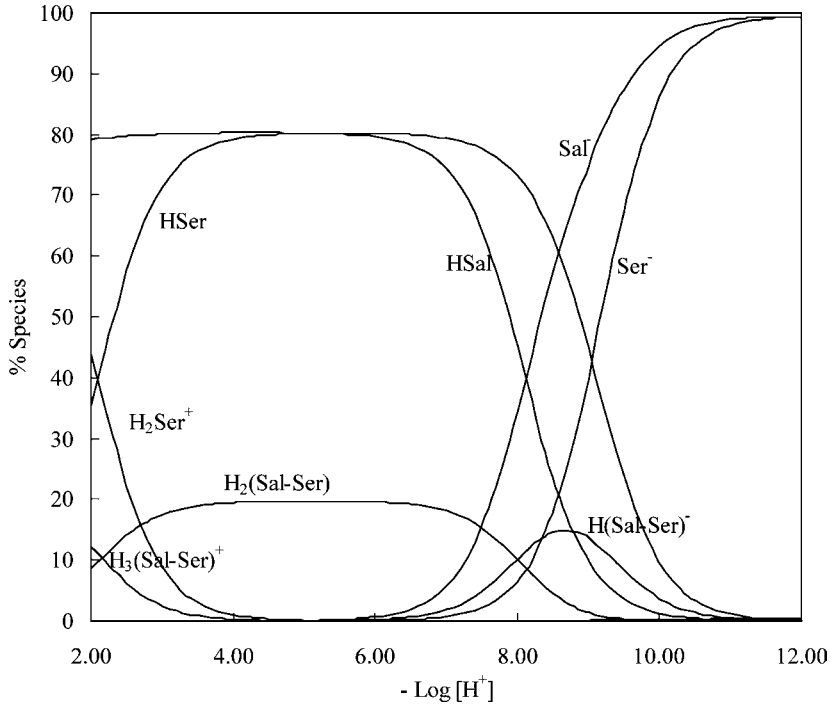


Fig 2. Species' distribution curves for the system, salicylaldehyde-serine, at a 1:1 molar ratio.

Schiff base is highest at p[H] = 9.0 and it is monoprotonated. (Sal-Ser^{2-} is given as an example Schiff base in Fig. 2). Extensive dissociation usually occurs in more acidic regions where both phenolate and carboxylate groups are protonated.

3.3. Metal Complexes of Schiff Bases

The potentiometric titration curves of Schiff bases and their M(II) complexes, together with the titration curve of the binary system M(II)/amino acid (taken as a representative of salicylideneserine) are shown in Figs. 3–5. By comparing the titration curves of the systems of M(II)/amino acid and M(II)/Schiff bases, it can be seen that the beginning of each curve of the system M(II)/Schiff base is nearly coincident with the beginning of the titration curve of the binary system M(II)/amino acid. This behavior can be explained by the fact that amino acids lose one proton at a lower pH, besides the fact that they bind more strongly to the metal ion. Beyond $a = 2$ for the system Cu(II)/Schiff base and $a = 3$ for the systems Ni(II)/Schiff base and Zn(II)/Schiff base $\{a =$ number of moles of base added per mole of Cu(II)$\}$, the curves of the M(II)/Schiff base were found to deviate considerably from the curves of M(II)/amino acid, due to the formation of a Schiff

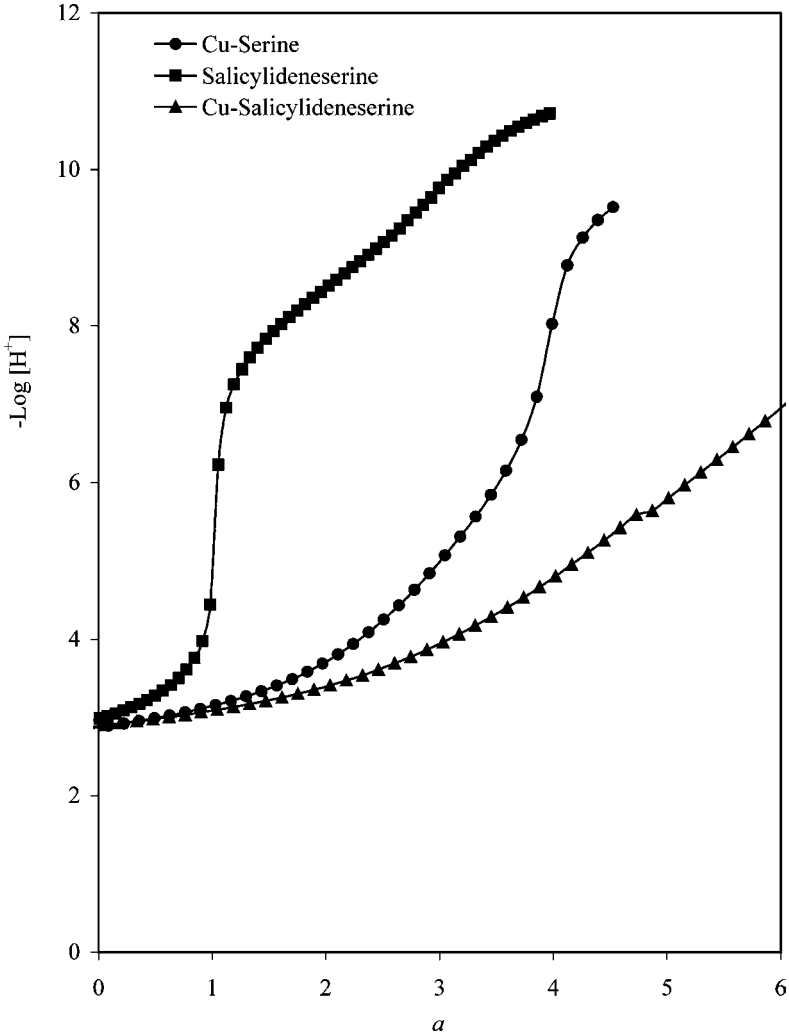


Fig 3. Potentiometric titration curves of the Cu(II)/serine and Cu(II)/salicylideneserine systems as a function of added KOH (a = moles of base added per moles of salicylideneserin or Zn(II)).

base metal complex. For the metal complex curves, there is a significant lowering from that of the free Schiff base, indicating formation of metal complexes by release of protons. The Schiff bases formed in this research serve as tridentate ligands by the coordination of the imine, phenoxide and carboxylate donor groups with the metal ion. It has been suggested that for such complexes the metal ion

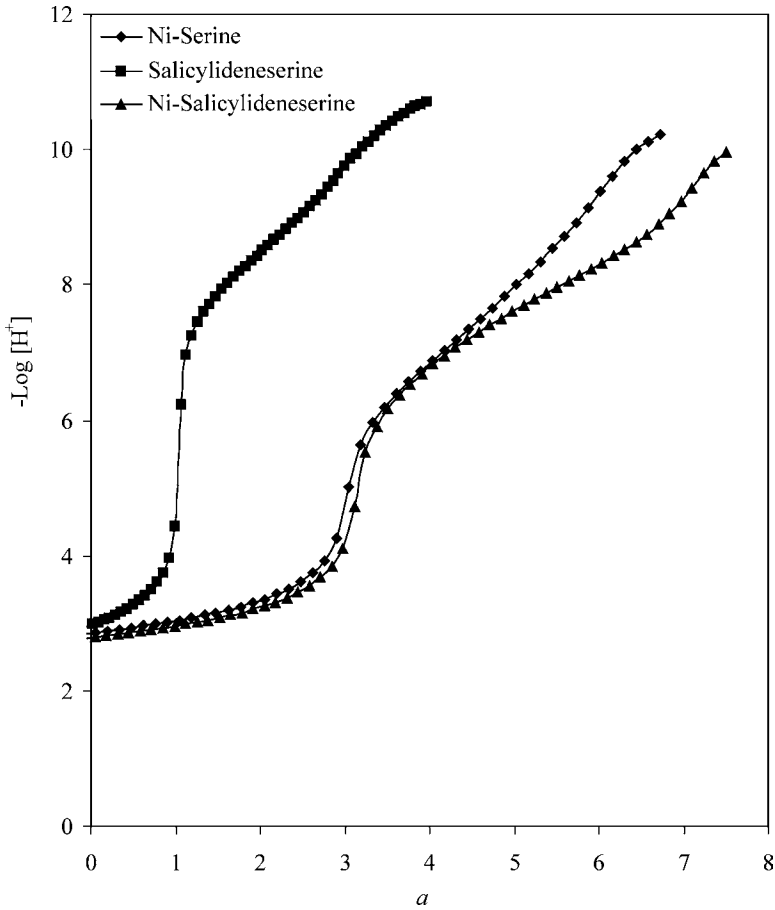


Fig 4. Potentiometric titration curves of the Ni(II)/serine and Ni(II)/salicylideneserine systems as a function of added KOH (a = moles of base added per moles of salicylideneserin or Zn(II)).

is more strongly coordinated to the imine nitrogen and phenoxide oxygen than to the carboxylate oxygen.[38]

The pH measurements were carried out for systems containing 1:1:1 and 1:1:0.5 molar ratios of the amino acid derivatives, salicylaldehyde and metal ion, respectively. The appearance of a precipitate even in weakly acidic solutions was a characteristic feature of the majority of the 1:1:1 systems. More useful information was obtained from the metal ions whereby the complex species formed were soluble over a large range of pH. The potentiometric data for the Cu(II)-Schiff base systems indicate that an insignificant tendency exists toward the formation

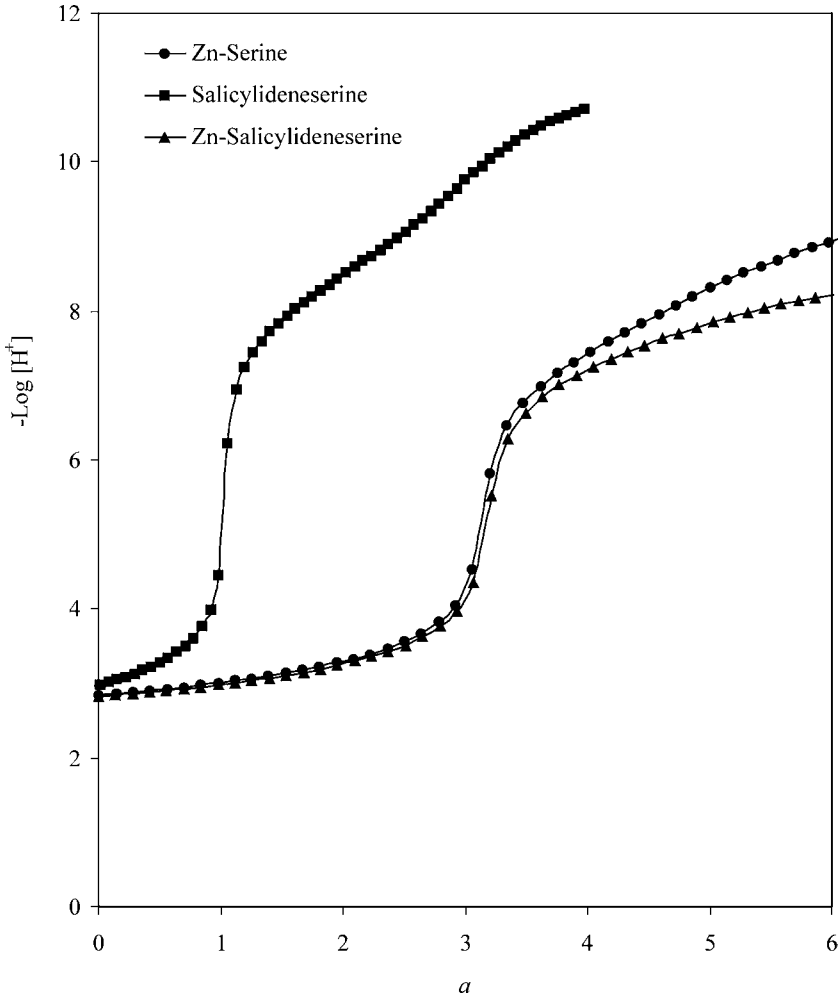


Fig 5. Potentiometric titration curves of the Zn(II)-serine and Zn(II)-salicylideneserine systems as a function of added KOH (a = moles of base added per moles of salicylideneserin or Zn(II)).

of $M(SB)_2$ species, whereas the data for the Zn(II) and Ni(II) systems suggested the formation of considerable amounts of these species in the case of Schiff bases derived from glycine, alanine, serine, phenylalanine and tyrosine.

The proposed species' model, which was used for each Schiff base system, is based on other similar Schiff base systems.[8,17,21] The binary species presented in Table I were also included and fixed in the model of Schiff base systems, but only the ternary species were refined by the BEST program. The stability constants

for the Schiff base/M(II) complexes are reported in Table II. The data obtained in aqueous medium are in good agreement with data available in the literature.[8,20,21]

Comparison of the data in Tables I and II indicates that Schiff base/metal complexes are significantly more stable than binary complexes having the corresponding stoichiometry. This may be caused by the fact that Schiff bases behave as tridentate ligands, each of which forms five- and six-membered fused two-ring systems.[39,40]

According to Table II, when log β_1^{Ni}, log β_2^{Ni}, log β_1^{Zn}, and log β_2^{Zn} values vary in the order, Sal-Gly > Sal-Ala > Sal-Ser > Sal-Tyr ≥ Sal-Phe, whereas the log β^{Cu} values vary as, Sal-Ala > Sal-Ser > Sal-Gly > Sal-Tyr ≥ Sal-Phe. These orders can explain the strength of the C=N bond, the basicity of the Schiff base and the steric effect.[21] If the rank of the stability constants and the formation and protonation constants is compared in order to investigate the influence of the first two factors, it is seen that there is correlation between them. The linear correlation coefficients, r, between the logarithms of the stability constants of the complexes and the formation and protonation constants of the ligands are set out in Table III. An inspection of the correlation coefficients (Table III) reveals that none of the stability constants correlates significantly with log K_2^H (log K_3^H for Sal-Tyr) and log K_3^H (log K_4^H for Sal-Tyr) and the values of the stability constants depend primarily on the basicity of the imine group of the Schiff bases. The negative correlation between the stability constants and the protonation constants of the imine group indicates that the complexation equilibria of metal ions are competitive. When a Schiff base releases a proton from the imine nitrogen, the metal ion can bond to it.

The order of the stability constants may be due to steric interactions caused by the bulky alkyl group attached to the amino acids. The presence of the bulky alkyl group on the α-carbon atom of the amino acids is seen to cause a small,

Table III. The Linear Correlation Coefficients Between Pairs of Variables[a,b]

Formation and protonation constants of Schiff bases	Stepwise stability constants of Schiff base complexes				
	Ni(II)		Cu(II)	Zn(II)	
	log K_{ML}	log K_{ML2}	log K_{ML}	log K_{ML}	log K_{ML2}
log β_0	0.833*	0.856*	0.898*	0.793	−0.981**
log K_1^H	−0.909*	−0.781	−0.882*	−0.833*	0.936*
log K_2^H	−0.442	−0.531	−0.377	−0.513	0.545
log K_3^H	0.431	0.133	0.226	0.532	−0.478

[a] The correlation coefficients were computed by SPSS.

[b] In each case, it was used five pairs of variables in calculation of correlation coefficients.

*Correlation is significant at the 0.05 level.

**Correlation is significant at the 0.01 level.

but measurable, decrease in the stability of their Schiff base complexes. This effect does not appear to arise from interactions of the alkyl group with other coordinated ligands, because the presence of bulkier ligands has little effect on the relative stability; the logarithms of the constants for reaction, $M(SB) + HSB \rightleftharpoons M(SB)_2 + H$ are −3.32, −3.29, -3.07, −3.87, −4.06 (M is Ni) and −4.56, −4.86, −4.33, −4.55, −4.87 (M is Zn) for Sal-Gly, Sal-Ala, Sal-Ser, Sal-Phe and Sal-Tyr, respectively. Probably the influence of the alkyl groups arises from its effects on the solvation of the complex and on the $=NCH(R)COO^-$ bond angle.[21]

Replacement of the proton bound to the azomethine nitrogen of a Schiff base by a divalent metal ion, except for Cu(II), does not seem to make a remarkable difference in the stability of the complex; the M(SB) chelates investigated have even lower formation constants than HSB. The stability sequences observed for the species M(SB) and $M(SB)_2$ are Cu(II) > Ni(II) > Zn(II). Thus, the Irving–Williams order of complexation, which is related to the ligand-field stabilization energies, is fulfilled.[41,42]

Estimation of the equilibrium concentrations of metal(II) complexes as a function of pH provides a useful picture of metal ion binding in biological systems. In all of the species' distributions, the concentration of the Schiff base metal complexes increases with increasing pH, thus making complex formation more favored in the physiological pH range (see Figs. 6–8). The species' distribution pattern for the Ni-Sal-Ser system indicates that Ni(Sal-Ser) starts to form at a pH ∼5 and reaches a maximum concentration (∼60%) at pH ∼ 7.5–9.5. In this pH range, $Ni(Sal\text{-}Ser)_2$ begins to form and is found with Ni(Sal-Ser) in solution. The predominant form is Ni(Sal-Ser). The distribution curve of the Zn-Sal-Ser system, in which the Schiff base complex starts to form at pH ∼6 and its concentration reaches a maximum (∼60%) at pH ∼ 8.0–9.0, is similar to the curve of Ni-Sal-Ser system. On the other hand, the distribution curve of the Cu-Sal-Ser system is quite different from the other two in that the formation of the Cu(Sal-Ser) complex begins at pH ∼ 2.5 and Cu(Sal-Ser) is the predominant species (∼98%) in the pH range 4–10. This difference, which results from the higher affinity of Cu(II) for nitrogen and oxygen donors, may be evidence that Cu(II) is most effective in catalyzing the deamination reactions, because these reactions proceed at an optimum rate between pH 4 and 5 and are negligible above pH 9.[43]

4. CONCLUSION

The present results may have important biological implications. To interpret properly the biological processes involving amino acids it is necessary to have quantitative data on all pertinent equilibrium constants [*i.e.*, the formation constants of the Schiff base, the protonation constants of the Schiff base, the stability constants of Schiff base metal complexes, and the protonation constants of the amino acids and salicylaldehyde from which the Schiff bases are derived as well

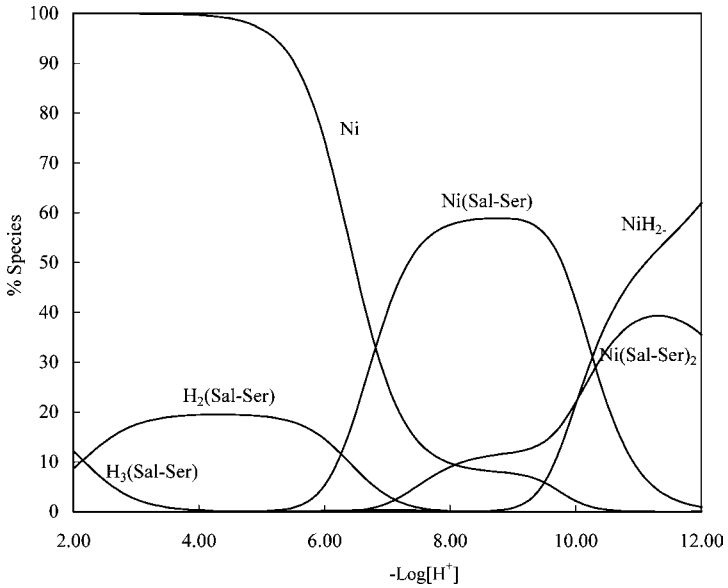


Fig 6. Species' distribution curves of the system, Ni(II)-salicylaldehyde-serine, at a 1:1:1 molar ratio.

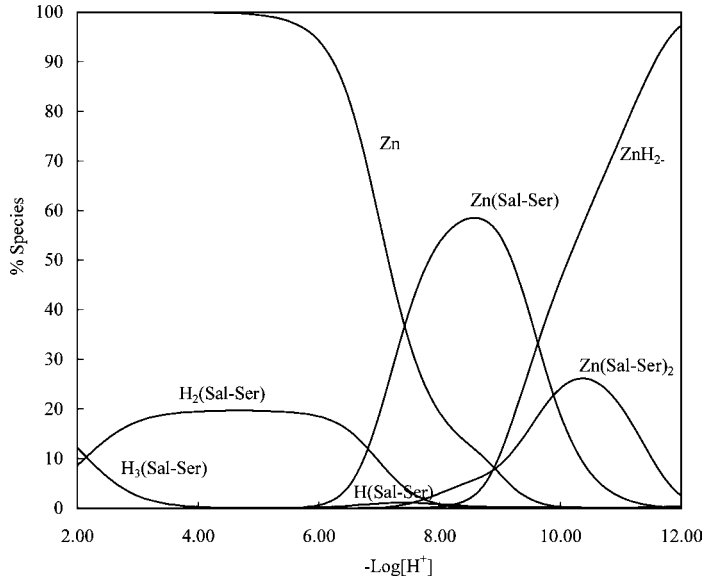


Fig 7. Species' distribution curves for the system, Zn(II)-salicylaldehyde-serine, at a 1:1:1 molar ratio.

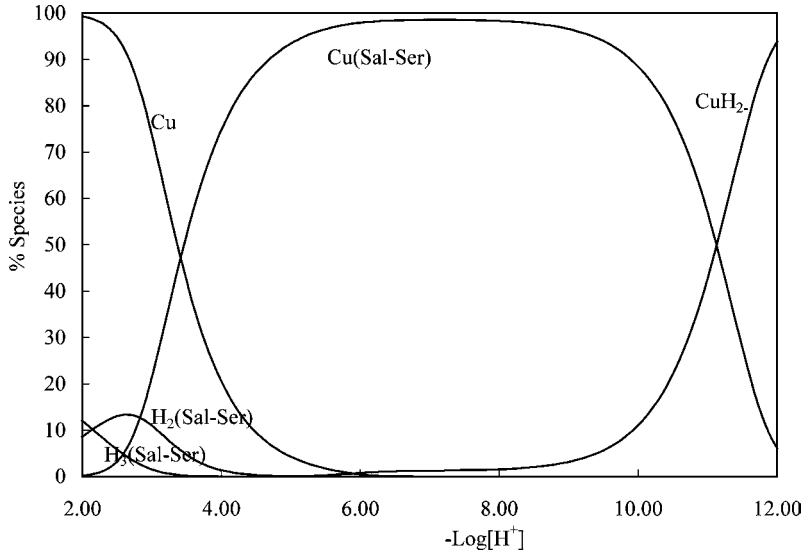


Fig 8. Species' distribution curves for the system, Cu(II)-salicylaldehyde-serine, at a 1:1:1 molar ratio.

as their metal binding constants]. By suitably varying the nature of the metal ion and the experimental parameters it should be possible to increase considerably our understanding of the chemical factors which are involved in more complicated biological processes.

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