Ternary Complex Formation between Chromium(III)−Picolinic Acid, Chromium(III)−Dipicolinic Acid, and Small Blood Serum Bioligands

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The complex species formed between chromium(III) picolinic and chromium(III) dipicolinic acids and small blood serum bioligands such as lactic, oxalic, citric, and phosphoric acids were studied in aqueous solution by means of electromotive force measurement emf(H) at 25 °C and 1.5 mol·dm^{-3} KCl as the ionic medium. The binary and ternary complexes were studied by the aging solution method, consisting of the preparation of different molar ligand/metal ratios at different pH values: solutions were maintained at room temperature (25 ± 1 °C) for 45 days; potentiometric measurements were then done; and the data were analyzed by means of the least-squares computational program LETAGROP, obtaining the respective stability constants and the stoichiometric coefficients of the complexes formed in aqueous solution.

Introduction

In 1959, chromium was identified as the active component of the "glucose tolerance factor" (GTF). In fact, the symptoms of glucose intolerance are characterized by high glucose and insulin levels, which are considered as a sign of chromium deficiency. Chromium supplements play nutritional roles and can prevent or reduce clinical symptoms. In fact, supplements of organic chromium(III) complexes exist that are recommended for use in the treatment of diabetes and in patients with high cholesterol levels. In 1980, the National Research Council and the National Academy of Sciences recommended a daily 50−200 μg consumption of chromium(III).[1]

The trispicolinatechromium(III) complex, [Cr(pic)$_3$], is a known bioavailable source of chromium(III), which provides 2−5 % of this absorbable bioelement, where the picolinate acts as a Cr(III) transporter.[2,3]

The Cr(III) dipicolinic acid (H_2Dipic) can also be used as an alternative to Cr(III) supplements, first because of its similarity with picolinic acid (HPic) and also because of the physiological properties shown by this ligand. These pyridinecarboxylic ligands are of great importance because of their presence in many natural products: alkaloids, vitamins, and coenzymes.[4]

After oral administration of these complexes, they may encounter many other potential chromium(III) binding molecules, available in extracellular or intracellular biological fluids. These latter ligands may partially or completely displace the original chromium(III) carrier molecules from the coordination sphere of the metal. Accordingly, ternary complex formation should be taken into account in a speciation description of these complexes in biological fluids. Such ternary complexes might be of great importance in the absorption and transport processes of Cr(III)−picolinic and Cr(III)−dipicolinic acid complexes and even in their physiological activity.[5]

Because of the inertness of the Cr(III) ion,[6] complex formation reactions are too slow. Alternatives to overcome this problem include either increasing the temperature[7] or aging the solution at a certain temperature.[8]

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In this paper, we report the binary and ternary complexes formed between the Cr(III) picolinic and Cr(III) dipicolinic acids with the small blood serum bioligands, lactic acid (Lac), oxalic acid (Ox), citric acid (Cit), and phosphoric acid (Phos), preparing mixtures of metal ligands at different molar ratios and aging the solution at room temperature (25 ± 1 °C) for 45 days. Finally, the pH of the solutions was measured.[9] These experiments were done as a contribution to the speciation of chromium(III) in aqueous solution.

Experimental Section

Chemicals. All ligands were Merck products of puriss quality and were used as received. The stock lactate solution was prepared by dilution of sodium lactate solution (50 % water solution). Ligand stock solutions were prepared at 25 mmol·dm^{-3} concentration, and the $CrCl_3$ stock solution (10 mmol·dm^{-3}) was prepared by dissolution of $CrCl_3$·6H_2O. The hydrogen ion concentration was determined by using the appropriate Gran function.[10] The HCl and KCl solutions were prepared by dissolving the respective acids and salts (Merck, analytical grade) in twice distilled water which was previously boiled to remove dissolved CO_2. A carbonate-free hydroxide solution (KOH) was prepared from a Titrisol Merck ampule and standardized against potassium hydrogen phthalate. The emf(H) measurements were carried out in aqueous solution at an ionic strength of 1.5 mol·dm^{-3} using KCl. Argon free of O_2 and CO_2 was used.

Titration Procedure. The stability constants of the proton and Cr(III) binary and ternary complexes were determined by pH-potentiometric titration. The ionic strength was adjusted to 1.5 mol·dm^{-3} KCl in each solution studied. In all cases, the temperature was 25.0 ± 0.1 °C. The pK_a of the ligands was determined according to the method previously reported.[11] The total Cr(III) concentration was maintained in the range of 2−3 mmol·dm^{-3}, and the molar ratios in the Cr(III) binary systems were 1:1, 1:2, and 1:4. For the ternary systems, the ratios of metal ion, ligand A (Pic and Dipic), and ligand B (Lac, Ox, Cit, and Phos) were 1:1:1, 1:1:2, and 1:2:1. All titrations were performed over the pH range 1−8 or until precipitation occurred.

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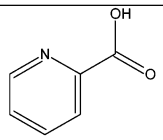
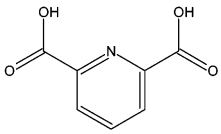
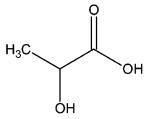
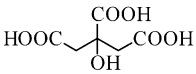
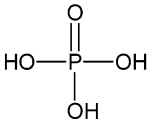
Table 1. Acid Dissociation Constants in Aqueous Media (I = 1.5 mol·dm^{-3} KCl at 25.0 ± 0.5 °C)

name of ligands	chemical structure (neutral form)	pK_{a1}	pK_{a2}	pK_{a3}	ref
Picolinic Acid (Pic)		1.31 ± 0.03	5.26 ± 0.02		This work
		1.26[a]	5.62[a]		15
Dipicolinic Acid (Dipic)			2.30 ± 0.02	4.52 ± 0.03	This work
		0.49[b]	2.18[b]	4.62[b]	16
Lactic Acid (Lac)		3.69 ± 0.02			This work
		3.597[c]			17
Oxalic Acid (Ox)	HOOC−COOH	1.27± 0.02	3.61± 0.02		This work
		0.89[c]	3.52[c]		18
Citric Acid (Cit)		3.00 ± 0.02	4.33 ± 0.03	5.40± 0.04	This work
		2.63[d]	4.11[d]		19
Phosphoric Acid (Phos)		1.69 ± 0.02	6.37 ± 0.03	11.0 ± 0.1	This work
		2.36[e]	6.61[e]	11.1[f]	20

Note: [a] 3.0 M KCl, [b] 1.0 M $NaClO_4$, [c] 1.0 M NaCl, [d] 1.0 M KNO_3, [e] 1.0 R_4NX.

The solutions were kept at room temperature (25 ± 1 °C) for 45 days, and after this period the potentiometric measurement was performed. The reproducibility of the titration points included in the evaluation was within 0.005 pH units throughout the whole pH range. The pH was measured with a Thermo Orion 520 A instrument equipped with a Orion Ross 8102BN pH electrode, calibrated for hydrogen ion concentration. A pK_w value of 13.84 ± 0.03 was determined and used for the calculations. The concentration stability constants of the binary $\beta_{pqr} = [M_pH_qL_r]/[M]^p[H]^q[L]^r$ and the ternary $\beta_{pqrs} = [M_pH_qL_rB_s]/[M]^p[H]^q[L]^r[B]^s$ complexes were calculated with the aid of the LETAGROP computer program.[12−14] During the calculations, the following Cr(III)−hydroxo complexes were assumed: $[Cr_6(OH)_{12}]$ (log $\beta_{6-12} = -30.3 \pm 0.1$), which was the only hydroxo complex observed under these experimental conditions.

Results and Discussion

Acidity Constants for Ligands. The ligand pK_a values were determined using the LETAGROP program at I = 1.5 mol·dm^{-3} in KCl. The pK_i values obtained are listed in Table 1, and the species distribution diagrams are given in Figure 1. The values obtained are in good agreement compared with other literature data at different ionic strengths and temperatures.[15−20,24]

Stability Constants of Binary Complexes. In Table 2, the results of the binary complexes studied in this work are summarized. The respective species distribution diagrams are given in Figure 2. The complexes [ML], [ML(OH)], and $[M_2(OH)_2L_4]$ were detected in the Cr(III)−Pic system. Chiacchierini et al.[21] studied this system by spectrophotometric measurements and reported the formation of the complexes $[MHL]^{3+}$, $[MHL_2]^{2+}$, $[CrL_2]^+$, and $[CrL_3]$. In Figure 2A is presented the distribution diagrams for this system: it is observed that the [ML] complex is abundant in the pH range 2.4−3.3, and at pH > 3.5, the dimeric complex $[M_2(OH)_2L_4]$ is the most important species. This complex is a μ-dihidroxo complex that has been synthesized before,[22] where the four picolinate molecules act as bidentate ligands by (N, COO^-) coordination. It is important to mention that with this method we have not found evidence for the formation of the $[ML_2]$ and $[ML_3]$ complexes. If we tried to include these complexes, the final fitting obtained was worse, so it demonstrated that the system evolved until the formation of the most stable products in the aqueous solution.

The analysis of the Cr(III)−Dipic system shows the formation of the $[MHL]^{2+}$, $[ML]^+$, [ML(OH)], and $[ML_2]^-$ complexes. Chiacchierini et al.[23] reported only the formation of two complexes $[MHL]^+$ and $[M(HL)_2]^+$. We tried this model, but the fitting was worse than the model finally obtained under our experimental conditions. The species distribution diagrams (Figure 2B) show that the $[CrHL]^{2+}$ is the most important species between pH 1 and 3, that the $[ML]^+$ and [ML(OH)] complexes are formed in lesser extension, and that $[CrL_2]^-$ is the most important complex in the 3−5 pH range.

In the Cr(III)−Lac system, we observed the formation of the $[ML]^{2+}$, $[ML(OH)]^+$, and $[ML(OH)_2]$ complexes. Figure 2C shows the species distribution diagram of this system where it can be seen that Cr(III) dominates at pH < 2, that $[ML(OH)]^+$

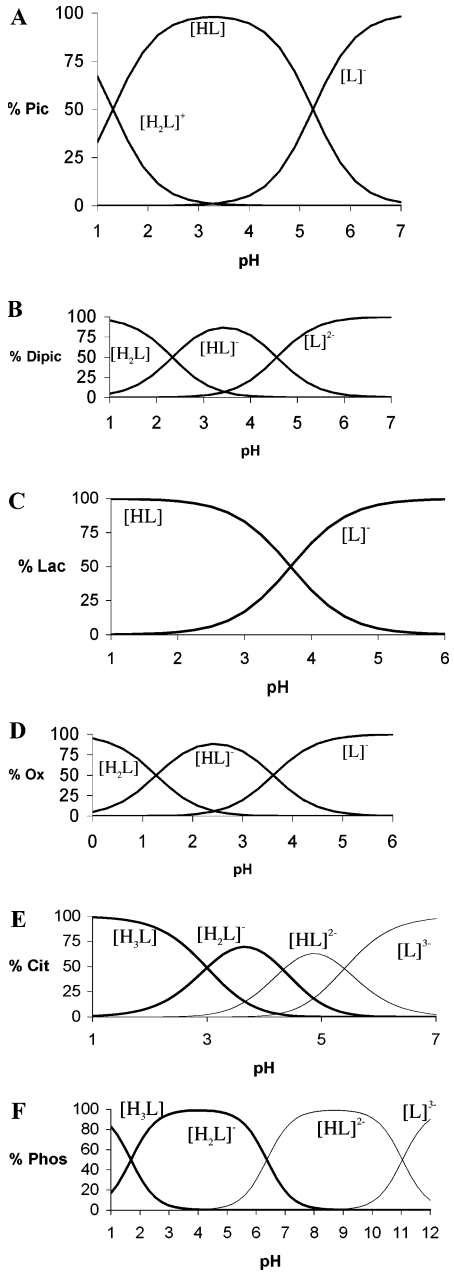


Figure 1. Species distribution diagrams for (A) Pic, (B) Dipic, (C) Lac, (D) Ox, (E) Cit, and (F) Phos in 1.5 mol·dm^{-3} at 25 °C.

forms between 2.2 < pH < 3, and that at pH > 4 the [ML-$(OH)_2$] complex is the most important species.

The $[ML]^+$, [ML(OH)], $[ML_2]^-$, $[ML_2(OH)]^{2-}$, and $[ML_3]$ complexes were obtained in the binary Cr(III)−Ox system. In previous studies, only the $[ML]^+$, $[ML_2]^-$, and $[ML_3]$ complexes were observed.[7,9] In Figure 2D is presented the species distribution diagram where it can be seen that the $[ML_3]$ complex is the most abundant species in the range 2.8 < pH < 6.5, whereas in the range 6.5 < pH < 9 the hydrolytic species [ML(OH)] and $[ML_2(OH)]^{2-}$ predominate.

In the Cr(III)−Cit system, the formation of the [ML], $[ML(OH)]^-$, $[MHL_2]^{2-}$, and $[ML_2]^{3-}$ complexes was observed. Tripathy and Patniak[25] reported the formation of the complexes [ML] and $[ML(OH)]^-$ and the dimer $[ML(OH)]_2^{2-}$. We tried to fit the experimental data considering this model, but the fitting obtained was worse than the model considered by us. Quiros et al.[26] obtained the crystal structure of the complex bispyridiniumbis(citrato)chromium(III) tetrahydrate, which contained a unit

Table 2. Stability Constants (log β) of Binary Cr^{3+}−Pic, Dipic, Lac, Ox, Cit, and Phos Complexes (I = 1.5 mol·dm^{-3} KCl at 25.0 ± 0.5 °C)[a]

ligand	species	log β	dispersion (σ)
Pic	ML	5.42 ± 0.09	0.042
		4.76[29]	
	ML(OH)	1.66 ± 0.2	
	$M_2(OH)_2L_4$	16.44 ± 0.2	
Dipic	MHL	9.52 ± 0.1	0.051
	ML	6.62 ± 0.1	
	ML(OH)	2.72 ± 0.1	
	ML_2	11.14 ± 0.2	
Lac	ML	3.89 ± 0.2	0.058
	ML(OH)	0.89 ± 0.1	
	$ML(OH)_2$	−2.91 ± 0.1	
Ox	ML	5.98 ± 0.1	0.049
		5.34[9]	
	ML(OH)	2.18 ± 0.1	
	ML_2	10.06 ± 0.3	
		10.51[9]	
	$ML_2(OH)$	4.86 ± 0.3	
	ML_3	13.74 ± 0.3	
		15.44[9]	
Cit	ML	6.53 ± 0.1	0.049
	ML(OH)	3.03 ± 0.09	
	M(HL)(L)	15.86 ± 0.2	
	ML_2	11.16 ± 0.1	
Phos	MHL	16.7 ± 0.1	0.033

[a] The binary complexes were studied according to the reaction scheme: $qCr^{3+} + rL + pH_2O \rightleftharpoons [Cr_q(OH)_p(L)_r] + pH^+$, $\beta_{p,q,r}$

of the $[ML_2]^{3-}$ complex, where the citrate is acting as a tridentate ligand by (COO^-, O^-, COO^-) coordination. Figure 2E shows the species distribution diagram of this system in which we can see that the complex $[ML(OH)]^-$ is the most important complex formed in solution.

In the Cr(III)−Phos system, the formation of a $[MHL]^+$ complex was detected. This is consistent with the results obtained by Lihiri and Aditya,[27] where they also reported the formation of this complex. It is important to say that only the data pH < 3 were used in the analysis of the potentiometric data because of the solubility problem at pH > 3.

The analysis of the ternary Cr(III)−Pic−Lac system (Table 3) shows the formation of two complexes [Cr(pic)(lac)(OH)] and $[Cr(pic)(lac)(OH)_2]^-$. We tried a three-complex model including the 1:1:1 $[Cr(pic)(lac)]^+$ complex, but the fitting obtained was worse than the two ternary complex model finally chosen. In the species distribution diagram (Figure 3A), a complicated mixture is observed at pH < 4, but at pH > 4, the ternary complex $[Cr(pic)(lac)(OH)_2]^-$ is the most important species.

In the Cr(III)−Pic−Ox system, only two ternary complexes were detected: $[Cr(pic)_2(ox)]^-$ and $[Cr(pic)(ox)_2]^{2-}$. This is consistent with the work of Kita and Laczna.[28] They studied the kinetics and the chelate ring-opening mechanism of some Cr(III)−Pic−Ox complexes, and they characterized in solution only two complexes, $[Cr(pic)_2(ox)]^-$ and $[Cr(pic)(ox)_2]^{2-}$, and proposed a formation mechanism of these complexes that involved the participation of deprotonated and protonated ligands. They concluded that the chelate ring opening depends on the electrical charge of the complex and is higher in $[Cr(pic)(ox)_2]^{2-}$ than $[Cr(pic)_2(ox)]^-$. This indicates that the two ox^{2-} ligands in the coordination sphere make the breaking of the Cr^{III}−N(pic) bond easier than in the monooxalate complex. Until now, we have not found in the literature reports of the formation of the 1:1:1 [Cr(pic)(ox)] complex. The species distribution diagram shows a complicated complex mixture in the pH range studied.

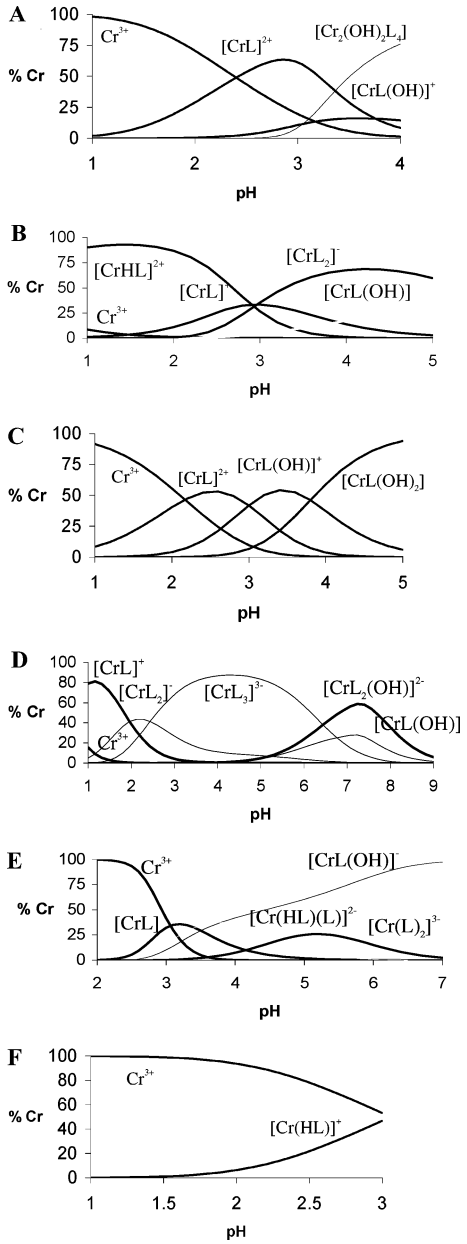


Figure 2. Species distribution diagrams for (A) Cr^{3+}−Pic, (B) Cr^{3+}−Dipic, (C) Cr^{3+}−Lac, (D) Cr^{3+}−Ox, (E) Cr^{3+}−Cit, and (F) Cr^{3+}−Phos complexes in 1.5 mol·dm^{-3} at 25 °C. Conditions (A), (B), (E), and (F): $M_T = 2$ mM and ligand/metal ratio $R = 2$. Conditions (C): $M_T = 3$ mM and ligand/metal ratio $R = 2$. Conditions (D): $M_T = 2$ mM and ligand/metal ratio $R = 4$.

The analysis of the Cr(III)−Pic−Cit system shows the formation of the complexes [Cr(pic)(Hcit)], [Cr(pic)(cit)(OH)]$^{2-}$, and [Cr(pic)(cit)(OH)$_2$]$^{3-}$. The species distribution diagram shows the predominance of the [Cr(pic)(Hcit)] complex in the range 1.8 < pH < 3. The [Cr(pic)(cit)(OH)]$^{2-}$ complex is abundant in the range 3 < pH < 5.5, and the [Cr(pic)(cit)(OH)$_2$]$^{3-}$ complex is the most important species at pH > 5.5.

In the Cr(III)−Pic−Phos system, the data analysis gave the formation of two complexes, [Cr(pic)(H$_2$PO$_4$)]$^+$ and [Cr(pic)(PO$_4$)]$^-$. The species distribution diagram (Figure 3D) shows that the ternary [Cr(pic)(H$_2$PO$_4$)]$^+$ complex predominates in the range 1 < pH < 3, whereas the [Cr(pic)(PO$_4$)]$^-$ complex is the most important species at pH > 3. Any attempt to include in the analysis the [Cr(pic)(HPO$_4$)] complex was unsuccessful in improving the fitting of the experimental potentiometric data.

Table 3. Stability Constants (log β) of Ternary Cr^{3+}−Pic−Ligand B (Ligand B = Lac, Ox, Cit, and Phos) and Ternary Cr^{3+}−Dipic−Ligand B Complexes (I = 1.5 mol·dm^{-3} KCl at 25.0 ± 0.5 °C)[a]

ligand	species	log β	dispersion (σ)
Pic	Lac		
	M(L)(B)(OH)	5.95 ± 0.2	0.096
	M(L)(B)(OH)$_2$	1.95 ± 0.1	
	Ox		
	M(L)(B)$_2$	15.8 ± 0.3	0.085
	M(L)$_2$(B)	15.02 ± 0.1	
	Cit		
	M(L)(HB)	18.3 ± 0.1	0.160
	M(L)(B)(OH)	12.49 ± 0.1	
	M(L)(B)(OH)$_2$	6.99 ± 0.3	
	Phos		
	M(L)(H$_2$B)	29.96 ± 0.2	0.179
	M(L)(B)	23.66 ± 0.2	
Dipic	Lac		
	M(L)(B)	13.21 ± 0.1	0.109
	M(L)(B)(OH)	9.41 ± 0.2	
	M(L)(B)(OH)$_2$	6.41 ± 0.1	
	Ox		
	M(L)(B)(OH)	10.3 ± 0.1	0.090
	M(HL)(B)$_2$	30.38 ± 0.2	
	M(L)(B)$_2$	19.3 ± 0.3	
	M(L)(B)$_2$(OH)	17.48 ± 0.2	
	Cit		
	ML(HB)	20.55 ± 0.2	0.134
	M(L)(B)	18.15 ± 0.2	
	M(L)(B)(OH)	13.85 ± 0.3	
	Phos		
	M(L)(HB)	23.02 ± 0.2	0.114
	M(L)(B)	17.22 ± 0.2	

[a] The ternary complexes were studied according to the reaction scheme: $qCr^{3+} + rL + sB + pH_2O \rightleftharpoons [Cr_q(OH)_p(L)_r(B)_s] + pH^+$, $\beta_{p,q,r,s}$

The analysis of the Cr(III)−Dipic−Lac ternary system shows the formation of three complexes, [Cr(dipic)(lac)], [Cr(dipic)(lac)(OH)]$^-$, and [Cr(dipic)(lac)(OH)$_2$]$^{2-}$. In Figure 3E the species distribution diagram is given, in which we observed the abundance of the [Cr(dipic)(lac)] complex in the range 1.3 < pH < 3.2. The [Cr(dipic)(lac)(OH)]$^-$ complex is formed in low quantity in the range 2.5 < pH < 4.5, and the [Cr(dipic)(lac)(OH)$_2$]$^{2-}$ complex is the most important species at pH > 3.5.

In the Cr(III)−Dipic−Ox ternary system four complexes were observed: [Cr(dipic)(ox)(OH)]$^{2-}$, [Cr(Hdipic)(ox)$_2$]$^{2-}$, [Cr(dipic)(ox)$_2$]$^{3-}$, and [Cr(dipic)(ox)$_2$(OH)]$^{4-}$. In Figure 3F, the species distribution diagram of this system is presented, which shows the existence of only ternary complexes, with the [Cr(Hdipic)(ox)$_2$]$^{2-}$ complex being the most important species in the range 1 < pH < 6. The [Cr(dipic)(ox)$_2$]$^{3-}$ complex is formed at maximum of 50 % at pH = 6.5, and at pH > 6.5, the [Cr(dipic)(ox)$_2$(OH)]$^{4-}$ complex is the most abundant species.

The analysis of the potentiometric data in the Cr(III)−Dipic−Cit system shows the formation of three complexes, [Cr(dipic)(Hcit)]$^-$, [Cr(dipic)(cit)]$^{2-}$, and [Cr(dipic)(cit)(OH)]$^{3-}$. In Figure 3G, the respective species distribution diagram is presented, from which it can be seen that the [Cr(dipic)(Hcit)]$^-$ complex is important in the range 1.5 < pH < 2.5, that the [Cr(dipic)(cit)]$^{2-}$ complex is formed to 80 % in the range 2.5 < pH < 4.2, and that the [Cr(dipic)(cit)(OH)]$^{3-}$ complex is the most important species at pH > 4.2.

In the Cr(III)−Dipic−Phos system, only two ternary complexes were detected: [Cr(dipic)(HPO$_4$)]$^-$ and [Cr(dipic)(PO$_4$)]$^{2-}$. In Figure 3H, the respective species distribution diagram is given. A mixture of binary Cr(III)−Dipic complexes and ternary complexes is observed; however, the [Cr(dipic)(HPO$_4$)]$^-$ complex is the most abundant species in the pH range 3.2 to 5.8,

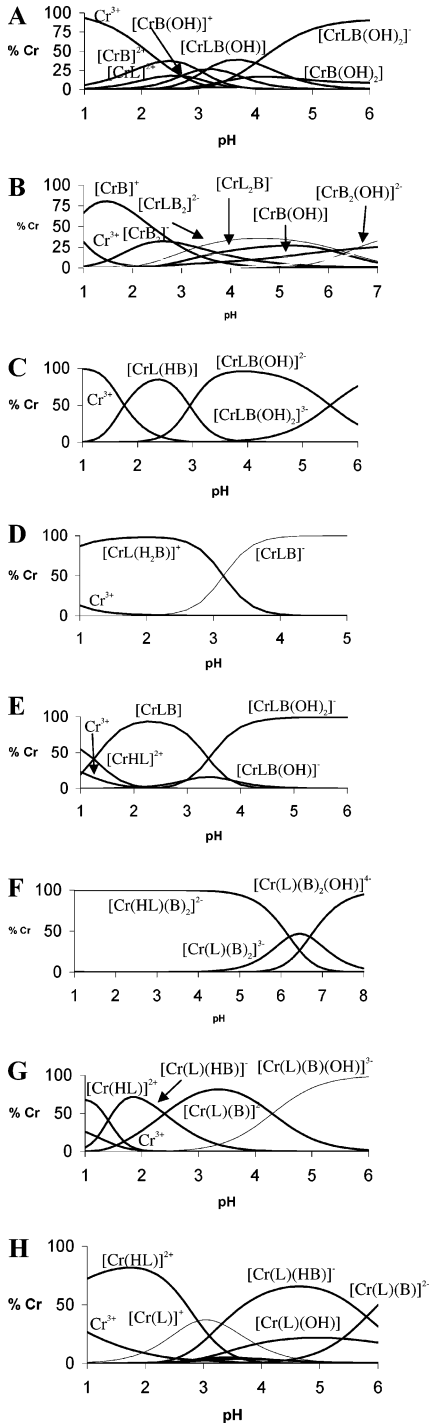


Figure 3. Species distribution diagrams for (A) Cr^{3+}−Pic−Lac, (B) Cr^{3+}−Pic−Ox, (C) Cr^{3+}−Pic−Cit, (D) Cr^{3+}−Pic−Phos, (E) Cr^{3+}−Dipic−Lac, (F) Cr^{3+}−Dipic−Ox, (G) Cr^{3+}−Dipic−Cit, and (H) Cr^{3+}−Dipic−Phos complexes in 1.5 mol·dm^{-3} at 25 °C. Conditions: $M_T = 2$ mM and Cr^{3+}/Pic/ligand B and Cr^{3+}/Dipic/ligand B ratios $R = 1:1:2$.

whereas the $[Cr(dipic)(PO_4)]^{2-}$ complex is abundant at pH > 5.8.

When the relative stability constant of the ternary complex, [Cr(dipic)(lac)], is compared to the binary ones, $[Cr(dipic)]^+$ and $[Cr(lac)]^{2+}$

$$[Cr(dipic)]^+ + [Cr(lac)]^{2+} \rightleftharpoons [Cr(dipic)(lac)] + Cr^{3+}$$

has a value of log $\beta = +2.7$, which means that the ternary complex is more stable than the binary ones.

> Although there are some empirical relationships between the stabilities of mixed ligand complexes and the corresponding parent complexes, a general and satisfactory theoretical explanation is still lacking. Statistically the formation of the mixed ligand specie is always favored... The experimentally determined stability constants in most cases deviate from the statistically calculated constants. Because most of the earlier determined constants showed that the stability of the mixed species is preferential, it was thought that the extra stabilization is a general phenomenon.[30]
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> M. T. Beck

Khalil[31−34] has done contributions on the study of ternary complexes, and he saw positive and negative deviations from the statiscal values.

Conclusions

Chromium(III) complex formation reactions are slow. The study of these complexes by an aging solution method for 45 days at 25 ± 1 °C gave us an idea of the most stable complexes formed in aqueous solution. In fact, in the Cr(III)−pic system, for example, only three complexes were detected, [ML], [ML(OH)], and $[M_2(OH)_2L_4]$, that are formed under these conditions, and when we tried to include the $[ML_2]$ and $[ML_3]$ complexes, the fitting obtained was worse, corroborating that this method may give a more realistic view of the most stable complexes formed in aqueous solution.

Acknowledgment

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Literature Cited

(1) Ding, H.; Olson, L.; Caruso. Elemental speciation for chromium in chromium picolinate products. *J. Spectrochim. Acta Part B* **1996**, *51*, 1801−1812.

(2) Chakov, N.; Collins, R.; Vincent, J. A re-investigation of the electronic spectra of chromium(III) picolinate complexes and high yield synthesis and characterization of $Cr_2(\mu\text{-}OH)_2(pic)_4{\cdot}5H_2O$ (Hpic = picolinic acid). *Polyhedron* **1999**, *18*, 2891−2897.

(3) Vincent, J. The bioinorganic chemistry of chromium(III). *Polyhedron* **2001**, *20*, 1−26.

(4) Mohamed, M. K.; Abeer, E. A. Potentiometric studies on the formation equilibria of binary and ternary complexes of some metal ions with dipicolinic acid and amino acids. *J. Chem. Eng. Data* **2000**, *45*, 1108−1111.

(5) Kiss, E.; Garriba, E.; Micera, G.; Kiss, T.; Sakurai, H. Ternary complex formation between VO(IV)−picolinic acid or VO(IV)−6-methylpicolinic acid and small blood serum bioligands. *J. Inorg. Biochem.* **2000**, *78*, 97−108.

(6) Purcel, K. F.; Kotz, J. C. *Inorganic Chemistry*; W. B. Saunders Company: Philadelphia, 1977; pp 694−755.

(7) Ciavatta, L.; Iuliano, M.; Vitielo, A. Stability constants of chromium(III) oxalate complexes in 1 M $NaClO_4$ at 60 °C. *Ann. Chim.* **2000**, *90*, 169−179.

(8) Ciavatta, L.; Grimaldi, M. On the hydrolysis of the iron(III) ion, Fe^{3+}, in perchlorate media. *J. Inorg. Nucl. Chem.* **1975**, *37*, 163−169.

(9) Nagata, K.; Umayahara, A.; Tsuchiya, R. Formation constants of chromium(III)−oxalato complexes. *Bull. Chem. Soc. Jpn.* **1965**, *38*, 1059−1061.

(10) Gran, G. Determination of the equivalence point in potentiometric titrations. *Part II Analyst* **1952**, *77*, 661−671.

(11) Armas, M. T.; Mederos, A.; Gili, P.; Domínguez, S.; Hernández-Molina, R.; Lorenzo, P.; Baran, E. J.; Araujo, M. L.; Lubes, V.; Brito, F. Speciation in the carnosine−oxovanadium(IV) system. *Polyhedron* **2002**, *21*, 1513−1521.

(12) Brauner, P.; Sillén, L. G.; Whiteker, R. High-speed computers as a supplement to graphical methods. 9. Adjustment for systematic experimental errors and other group parameters in Letagrop. Applications to potentiometric titrations. *Ark. Kemi.* **1969**, *31*, 365.

(13) (a) Brito, F. Project 14/02.06.87, Education Council, Canary Islands Government: Tenerife, Spain, 1987. (b) Brito, F.; Gonçalves. Project S1−1228, CONICIT, Caracas: Venezuela, 1981.

(14) Brito, F.; Araujo, M. L.; Lubes, V.; D'Ascoli, A.; Mederos, A.; Gili, P.; Domínguez, S.; Hernández, R.; Armas, M. T.; Baran, E. J. Emf-(H) data analysis of weak metallic complexes using reduced formation functions. *J. Coord. Chem.* **2005**, *58*, 501−512.

(15) Lubes, V. Vanadium(III) complexes with picolinic acid and dipicolinic acid in aqueous solution. *J. Solution Chem.* **2005**, *34*, 889−915.

(16) Funahashi, S.; Haraguchi, K.; Tanaka, M. Reactions of hydrogen peroxide with metal complexes. 2. Kinetic studies on the peroxo complex formation of nitrilotriacetatodioxovanadate(V) and dioxo-(2,6-pyridinedicarboxylato)vanadate(V). *Inorg. Chem.* **1977**, *16*, 1349−1353.

(17) Cruywagen, J. J.; Krüger, L.; Elisabeth A.; Rohwer, E. E. Molybdenum(VI) and tungsten(VI) complex formation. Part 5. The reaction with lactate in 1.0 mol dm^{-3} sodium chloride medium. *J. Chem. Soc., Dalton Trans.* **1993**, 105−110.

(18) Cruywagen, J. J.; Heyns, J. B.; van de Water, R. F. A potentiometric, spectrophotometric, and calorimetric investigation of molybdenum-(VI)−oxalate complex formation. *J. Chem. Soc., Dalton Trans.* **1986**, 1857−1862.

(19) Rajan, K. S.; Martell, A. E. Equilibrium studies of uranyl complexes. III. Interaction of uranyl ion with citric acid. *Inorg. Chem.* **1965**, *4*, 462−469.

(20) Irani, R. R.; Callis, C. F. Metal complexing by phosphorus compounds. IV. Acidity constants. *J. Phys. Chem.* **1961**, *65*, 934−937.

(21) Chiacchirini, E.; Campanella, L.; DeAngelis, G.; Petrone, V. The reaction between chromium(III) and picolinic acid. *Ann. Chim.* **1977**, *67*, 385−393.

(22) Stearns, D. M.; Armstrong, W. H. Mononuclear and binuclear chromium(III) picolinate complexes. *Inorg. Chem.* **1992**, *31*, 5178−5184.

(23) Chiacchirini, E.; D'ascenzo, G.; De angelis, G.; Magri', A. L.; Petrone, V. The reaction of chromium(III) with 2,X-pyridinecarboxylic acids. *Ann. Chim.* **1977**, *67*, 195−210.

(24) (a) Martell, A. E.; Smith, M.; Motekaitis, R. J. *NIST Critical stability constants of metal complexes database*; US Department of Commerce: Gaithersburg, MD, 1993. (b) Powell, K. J.; Pettit L. D. *IUPAC Stability Constants Database*; Academic Software: Otley, U.K., 1997.

(25) Tripathy, K. K.; Patnaik, R. K. Citrate complex of chromium. *J. Indian Chem. Soc.* **1966**, *43*, 772−780.

(26) Quiros, M.; Goodgame, D. M. L.; Williams, D. J. Crystal structure and EPR spectrum of bispyridinium bis(citrato)chromium(III) tetrahydrate. *Polyhedron* **1992**, *11*, 1343−1348.

(27) Lahiri, S. C.; Aditya, S. Chromium(III)−phosphoric acid complex. *J. Indian Chem. Soc.* **1966**, *43*, 513−517.

(28) Kita, E.; Laczna, M. Kinetics and mechanism of chromioum(III)−picolinate ring opening in some chromium(III)−oxalato−picolinato complexes in acidic aqueous solutions. *Trans. Metal Chem.* **2001**, *26*, 510−516.

(29) Takata, S.; Kyuno, E.; Tsuchiya, R. Formation constants of chromium-(III) complexes with (N,N)- (O,O)- and (N,O)-type ligands, and their relationship to structure. *Bull. Chem. Soc. Jpn.* **1968**, *41*, 3416−3418.

(30) Beck, M. T. *Chemistry of complex equilibria*; Van Nostrand Reinhold Company: Hungary, 1970; pp 174−207.

(31) Khalil, M. M. Solution Equilibria and Stabilities of Binary and Ternary Complexes with *N*-(2-Acetamido)iminodiacetic Acid and Ribonucleotides (AMP, ADP, and ATP). *J. Chem. Eng. Data* **2000**, *45* (5), 837−840.

(32) Khalil, M. M.; Attia, A. E. Potentiometric Studies on the Formation Equilibria of Binary and Ternary Complexes of Some Metal Ions with Dipicolinic Acid and Amino Acids. *J. Chem. Eng. Data* **2000**, *45* (6), 1108−1111.

(33) Khalil, M. M. Complexation Equilibria and Determination of Stability Constants of Binary and Ternary Complexes with Ribonucleotides (AMP, ADP, and ATP) and Salicylhydroxamic Acid as Ligands. *J. Chem. Eng. Data* **2000**, *45* (1), 70−74.

(34) Khalil, M. M.; Attia, A. E. Potentiometric Studies on the Binary and Ternary Complexes of Copper(II) Containing Dipicolinic Acid and Amino Acids. *J. Chem. Eng. Data* **1999**, *44* (2), 180−184.

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