Short Communication

# Stability constants of mixed ligand complexes of vanadium(III) with 8-hydroxyquinoline and the amino acids glycine, proline, α-alanine and β-alanine

William Sanoja [a], José Daniel Martínez [a], Mary Lorena Araujo [a], Felipe Brito [a], Lino Hernández [b], Edgar Del Carpio [b], Vito Lubes [b,*]

[a] Centro de Equilibrios en Solución, Escuela de Química, Facultad de Ciencias, Universidad Central de Venezuela (UCV), Caracas, Venezuela
[b] Departamento de Química, Universidad Simón Bolívar (USB), Apartado 89000, Caracas 1080 A, Venezuela

### ARTICLE INFO

### ABSTRACT

In this work we report the results of the investigation on the formation of ternary complexes in vanadium(III)–8-hydroxyquinoline (H8HQ) and amino acid glycine (HGly, HL), proline (HPro, HL), αalanine (HαAla, HL) and βalanine (HβAla, HL) systems. The analysis of the potentiometric data with the least-squares program LETAGROP indicates the formation of the complexes $[V(8HQ)(HL)]^{2+}$ and $V(8HQ)(L)(OH)$ in all the systems studied. The species distribution diagrams were briefly discussed.

## 1. Introduction

8-Hydroxyquinoline (H8HQ) is an organic compound which is a derivative of the heterocycle quinoline by placement of an OH group on carbon number 8. This compound is widely used commercially. It is a monoprotic bidentate chelating agent in neutral solution, the hydroxyl is in the protonated form ($pK_a = 9.89$) and the nitrogen is not protonated ($pK_a = 5.13$).

The reaction of 8-hydroxyquinoline with aluminium(III) results in $Al(8HQ)_3$, a common component of organic light-emitting diodes (OLEDs). Variations in the substituents on the quinoline rings affect its luminescence properties.

Even though vanadium(III) chemistry has not been so studied as vanadium(IV) or vanadium(V), it is important because the different applications observed in the literature, for example the vanadium(III) cysteine complexes have some antitumoral activity [1,2] and the vanadium(III) maltolate [3] and vanadium(III) dipicolinate complexes [4] have shown some insulin-mimetic activity.

The role of mixed ligand complexes in biological processes has been well recognized. The stabilities of mixed chelates are of great importance in biological systems as many metabolic and toxicological functions are dependent upon this stability. Many attempts have been made to correlate the stability of the metal–ligand complexes with their antimicrobial activity [5].

It is well established that ternary complexes play a decisive role in the activation of enzymes and also in the storage and transport of active substances [6]. Ogunniran et al. [7] have proved that physical properties and antimicrobial activities are enhanced upon complexation. It has been found that a majority of the metal complexes with 8-hydroxyquinoline possess biological activity [8–10]. Amino acids are well known for their tendency to form complexes with metals having biological significance and metabolic enzymatic activities [11].

The idea of this study is that after oral administration of the binary complexes, they may encounter many other potential vanadium(III) binding molecules present in extracellular or intracellular biological fluids. These latter ligands may partially or completely displace the original vanadium 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 process of the vanadium complexes and even in their physiological activity [12].

* Corresponding author at: Departamento de Química, Universidad Simón Bolívar (USB), Valle de Sartenejas, Apartado 89000, Caracas 1080 A, Venezuela. Tel.: +58 212 906 39 84; fax: +58 212 906 39 61.

E-mail address: lubesv@usb.ve (V. Lubes).

To the best of our knowledge, there are no reports on the speciation of ternary vanadium(III)–8-hydroxyquinoline complexes with the amino acids glycine (HGly, HL), proline (HPro, HL), αalanine (HαAla, HL) and βalanine (HβAla, HL) [13,14].

In this work we report the results of mixed ligand complex formation in V(III)–8-hydroxyquinoline–amino acid glycine (HGly, HL), proline (HPro, HL), αalanine (HαAla, HL) and βalanine (HβAla, HL) systems. The pH-potentiometry technique was used to determine the stoichiometries and stability constants of the complexes formed in aqueous solution.

## 2. Experimental

### 2.1. Reagents

$VCl_3$ (Merck p.a.) and 8-hydroxyquinoline (H8HQ) (Merck p.a.), and the amino acids glycine (HGly, HL), proline (HPro, HL), αalanine (HαAla, HL) and βalanine (HβAla, HL) (Merck p.a.), were used without purification. The solutions of HCl, $VCl_3$, KCl and the amino acids HL were prepared by dissolving the respective amino acid and salts (Merck, analytical grade) in triply glass-distilled water which had been boiled in order to remove dissolved $CO_2$. To avoid hydrolysis of the $VCl_3$ solution it was acidified with known amounts of HCl (200 mmol·dm$^{-3}$). A carbonate free KOH solution was prepared from an ampoule of Titrisol Merck and standardized against potassium hydrogen phthalate. The Emf(H) measurements were carried out in aqueous solution at ionic strength 3.0 mol·dm$^{-3}$ in KCl.

### 2.2. Methods

The Emf(H) measurements were done using the following instruments: Thermo Orion model 520A pH meter, Metrohm EA 876-20 titration vessel, and Lauda Brinkmann RM6 thermostatic bath. The sealed 100 mL thermostatted double-walled glass titration vessel was fitted with a combined Orion Ross 8102BN pH electrode with a titrant inlet, a magnetic stirrer, and an inert nitrogen atmosphere inlet with outlet tubes. The temperature was maintained at 25.0 (1) °C by constant circulation of water from the thermostat bath.

The Emf(H) measurements were carried out by means of the REF//S/ GE cell, where REF = Ag, AgCl/3.0 mol·dm$^{-3}$ KCl; S = equilibrium solution and GE = glass electrode. At 25 °C the Emf (mV) of this cell follows the Nernst equation, $E = E^0 + jh + 59.16 \log h$, where $h$ represents the free hydrogen ion concentration, $E^0$ is the standard potential and $j$ is a constant which takes into account the liquid junction potential [15]. The experiments were carried out as follows: a fixed volume of 0.100 mol·dm$^{-3}$ HCl was titrated with successive additions of 0.100 mol·dm$^{-3}$ KOH until near neutrality in order to get the parameters $E^0$ and $j$. Then, aliquots of H8HQ, the amino acid HL and an aliquot of the vanadium(III) stock solution were added sequentially. Finally, the titration was continued with 0.100 mol·dm$^{-3}$ KOH. The measurements were done using a total metal concentration, $M_T$ = 2–3 mmol·dm$^{-3}$ and vanadium(III):H8HQ:amino acid HL molar ratios R = 1:1:1, 1:2:1 and 1:1:2.

The $V^{3+}$–H8HQ–amino acid HL systems were studied according to the reaction scheme:

$$pH_2O + qV^{3+} + rH8HQ + sHL \rightleftharpoons [V_q(OH)_p(H8HQ)_r(HL)_s] + pH^+, \beta_{p,q,r,s}$$

where HL represents the amino acids: HGly, HPro, HαAla and HβAla, and $[V_q(OH)_p(H8HQ)_r(HL)_s]$ is the ternary (p, q, r, s) complex and $\beta_{pqrs}$ is the respective stability constant.

The potentiometric data were analyzed using the program LETAGROP [16,17] in order to minimize the function $Z_B = (h − H) / M_T$, where $H$ is the total (analytical) concentration of $H^+$, $h$ represents the equilibrium concentration of $H^+$, and $M_T$ represents the total (analytical) concentration of $V^{3+}$. Equilibria corresponding to the formation of the

**Table 1**
Ligand acidity constants (log $\beta_{pr}$) in 3.0 mol·dm$^{-3}$ KCl at 25 °C.

| Equilibrium | log $\beta_{pr}$ | | | | |
|---|---|---|---|---|---|
| | H8HQ | HGly | HPro | HαAla | HβAla |
| HL + H$^+$ ⇌ H$_2$L$^+$ | 5.47 (1) | 2.81 (2) | 2.73 (3) | 2.29 (2) | 4.10 (2) |
| HL ⇌ L$^-$ + H$^+$ | | −9.87 (2) | −10.05 (2) | −10.73 (3) | −10.32 (4) |
| Dispersion σ (Z) | 0.007 | 0.019 | 0.028 | 0.018 | 0.021 |
| | | | | | |
| p$K_i$ | | | | | |
| H$_2$L$^+$ − HL | 5.47 | 2.81 | 2.73 | 2.29 | 4.10 |
| HL − L$^-$ | | 9.87 | 10.05 | 10.73 | 10.32 |

Values in parentheses are standard deviations [3σ(log β)] on the last significant figure.

hydroxo complexes of V(III) were considered in the calculation of the stability constants of the ternary complexes. The following species were assumed: $[V(OH)]^{2+}$, log $\beta_{1,−1}$ = −3.07(3); $[V_2O]^{4+}$, log $\beta_{2,−2}$ = −3.94(2); and $[V_2O(OH)]^{3+}$, log $\beta_{2,−3}$ = −7.87 (9) [18]. In the case of the V(III)–H8HQ system [19], the V(III)–HGly system [20], and the V(III)–HPro system [21], V(III)–HαAla and V(III)–HβAla systems [22] were previously studied in our group.

The stability constant of the V(III) hydroxo complexes, the stability constants of the ligands and the stability constants of the binary complexes were kept fixed during the analysis. The aim of the analysis was to find a complex or complexes giving the lowest sum of the errors squared, $U = \sum (Z_B^{exp} − Z_B^{calc})^2$, the fittings were done by testing different (p, q, r, s) combinations.

The species distribution diagrams were done with the computer program HYSS [23], yielding the $\beta_{pqrs}$ values, which are summarized in Table 2.

## 3. Results and discussion

### 3.1. Ionization constants of the ligands studied

The ionization constants (Table 1) in the ionic medium 3.0 mol·dm$^{-3}$ KCl are in good agreement with the literature values, considering the differences in ionic strength and ionic medium [13, 14]. For H8HQ, it was only possible to measure the p$K_a$ of the pyridinic group, since we observed precipitation problems at neutral pH, so we couldn't measure the corresponding p$K_a$ of the phenolic group. For the amino acid HL studied, the p$K_1$ corresponds to the dissociation of the carboxylic group and the p$K_2$ is the deprotonation of the amine group.

### 3.2. Ternary vanadium(III) complexes

The experimental data was analyzed using the program LETAGROP [16,17]. In Fig. 1 the results in the form of $Z_B$(pH) of the V(III)–H8HQ– HGly system are given, which is representative of all the systems studied. In this case the best fitting was obtained considering the formation of the ternary complexes $[V(8HQ)(HGly)]^{2+}$ and V(8HQ)(Gly)(OH),
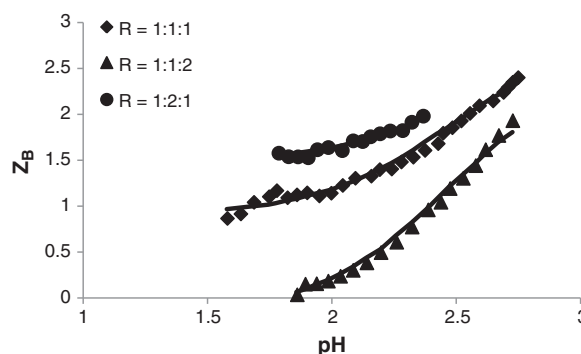


**Fig. 1.** $Z_B$ (pH) data of the $V^{3+}$–H8HQ–HGly system.

**Table 2**
Stability constants (log $\beta_{pqrs}$) of the V(III)–H8HQ–HL system (KCl 3.0 mol·dm$^{-3}$, 25 °C).

| Species | log $\beta_{pr}$ | | | |
|---|---|---|---|---|
| | HGly | HαAla | HβAla | HPro |
| [V(8HQ)(HL)]$^{2+}$ | 14.48 (4) | 14.34 (8) | 16.04 (7) | 14.73 (9) |
| V(8HQ)L(OH) | 9.72 (3) | 8.5 (1) | 10.28 (6) | 8.9 (1) |
| Dispersion ($\sigma$) | 0.055 | 0.080 | 0.068 | 0.088 |

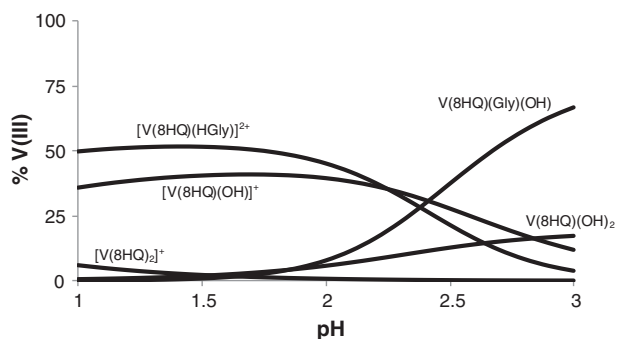Values in parentheses are standard deviations [$3\sigma(\log \beta_{pqrs})$] on the last significant figure.



**Fig. 2.** Species distribution diagrams of the V(III)–H8HQ–HGly system, considering that $M_T = 3$ mmol·dm$^{-3}$ and V$^{3+}$–H8HQ–HGly molar ratio R = 1:1:1.

and it is important to mention that the experimental data was obtained until pH < 3 because of the precipitation problem observed in all the system studied. The stability constants are summarized in Table 2. The species distribution diagrams are represented in Fig. 2.

It is important to say that in the analysis using the LETAGROP program, we tried to include the species [V(8HQ)(Gly)]$^+$ but the fitting obtained was worse, for this reason was considered the formation of two ternary complexes [V(8HQ)(HGly)]$^{2+}$ and V(8HQ)(Gly)(OH) in all the V(III)–H8HQ–HL systems studied in this work.

In Fig. 2 the species distribution diagrams for the conditions R = 1:1:1 and $M_T = 3$ mmol·dm$^{-3}$ of the V(III)–H8HQ–HGly system are given. We can see the predominance in 50% of the ternary complex [V(8HQ)(HGly)]$^{2+}$ at pH < 2.2 and, at pH > 2.3 the complex V(8HQ)(Gly)(OH) predominates. In addition, we can also observe in the figure the presence of the binary complexes [V(8HQ)(OH)]$^+$ and V(8HQ)(OH)$_2$ which are formed in less extension.

## 4. Conclusions

In this work we have studied the speciation of the ternary vanadium(III)–H8HQ–amino acid system, where the amino acids

studied were glycine (HGly), proline (HPro), αalanine (HαAla) and βalanine (HβAla). The data analyzed using the least-squares computational program LETAGROP indicate the formation of the complexes [V(8HQ)(HL)]$^{2+}$ and V(8HQ)(L)(OH) in all the systems studied.

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