5-ACETIL-8-HIDROXIQUINOLINA E 5-FORMIL-8-HIDROXIQUINOLINA: AGENTES CHELANTES PARA TITULAÇÕES COMPLEXOMÉTRICAS

5-ACETYL-8-HYDROXYQUINOLINE AND 5-FORMYL-8-HYDROXYQUINOLINE: CHELATING AGENTS FOR COMPLEXOMETRIC TITRATIONS

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RESUMO

Complexos metal-ligantes orgânicos são essenciais para muitos desenvolvimentos tecnológicos, desde montagens supramoleculares de proteínas até extração por solventes, titulações complexométricas e remediação ambiental. Foram estudadas as propriedades quelantes e ácido-base em etanol de dois derivados de 8-hidroxiquinolina (Q), 5-acetil-8-hidroxiquinolina (A) e 5-formil-8-hidroxiquinolina (F), das quais aplicações como quelantes são desconhecidas. A acidez dos ligantes seguiu a ordem **F** (pK_{a1} 2.9; pK_{a2} 9.5)> **A** (pK_{a1} 4.8; pK_{a2} 9.6)> Q (pK_{a1} 5.3; pK_{a2} 10.0) devida aos efeitos indutivos de grupos eletronegativos, formila em **F** e acetila em **A**. A maior acidez de **F** em relação a **A** foi devida à maior eletronegatividade do grupo formila em **F**. Esta ordem de acidez foi refletida nas maiores constantes de formação de complexos F-metal com valores de pKf de 32 (Fe^{3+}), 27,1 (Cu^{2+}), 26,2 (Zn^{2+}) e 24,9 (Pb^{2+}), do que com **A**, com valores pKf de 31, 22,5, 21,4 e 21.2 com estes metais, ou os valores de pKf na literatura para **Q**. Em resumo, **A** e **F** resultaram em excelentes quelantes para metais em titulações complexométricas com grandes constantes de formação; estas grandes constantes de formação recomendam a aplicação destes compostos em mascaramento, pré-concentração e titulação de metais por complexação e reações de oxidação-redução.

Palavras-chave: hidroxiquinolina, titulações complexométricas, constantes de dissociação, constantes de formação, absorividades molares

ABSTRACT

Metal–organic ligand complexes are essential to many technological developments from protein supramolecular assemblies to solvent extraction, complexometric titrations, and environmental remediation. We studied the chelating and acid-base properties in ethanol of two derivatives of 8-hydroxyquinoline (**Q**), 5-acetyl-8-hydroxyquinoline (**A**) and 5-formyl-8-hydroxyquinoline (**F**), of which applications as chelators are unknown. The ligands acidity followed the order **F** (pK_{a1} 2.9; pK_{a2} 9.5)> **A** (pK_{a1} 4.8; pK_{a2} 9.6)> **Q** (pK_{a1} 5.3; pK_{a2} 10.0) due to inductive effects of electronegative groups, formyl in **F** and acetyl in **A**. The higher acidity of **F** with respect to **A** was due to the higher electronegativity of the formyl group in **F**. This acidity order was reflected in larger formation constants of **F**-metal complexes with pK_f values of 32 (Fe^{3+}), 27.1 (Cu^{2+}), 26.2 (Cu^{2+}), and 24.9 (Pb^{2+}), than with **A**, with pK_f values of 31, 22.5, 21.4 and 21.2 with these metals, or the pK_f values in the literature for **Q**. In summary, **A** and **F** resulted excellent chelators for metals in complexometric titrations with large formation constants; these large formation constants recommend the application of these compounds in masking, preconcentration, and titration of metals by complexation and oxidation-reduction reactions.

Keywords: hydroxyquinoline, complexometric titrations, dissociation constants, formation constants, molar absorptivities

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INTRODUCTION

Complexometry of metals with organic ligands find applications in numerous scientific accomplishments including complexometric titrations, solvent extraction, preconcentration and other analytical applications, investigation in protein and nucleic acids supramolecular assemblies, and environmental remediation. **Q** derivatives with keto groups in position 5, such as **A** and **F** (Figure 1) have a hydroxyquinolinic system conjugated with a carbonyl group. Literature reports of **F**, **A**, and derivatives of these are limited. Among these, derivatives of **A**, 2-pyrazolines, oxazolines, pyridines, pyrimidines (Khalil *et al.*, 1991) and α,β-insaturated ketones containing aromatic or heterocyclic radicals (chalcones, which show a varied physiological activity) (Khalil *et al.*, 1991; Dhar, 1981; Balaji *et al.*, 2003; Patil *et al.*, 2009; Clemo and Howe, 1955; Matsumura *et al.*, 1960; Misra, 1973; Khalil *et al.*, 1988) are found. Furthermore, conjugation of the hydroxyquinolinic fragment and the highly reactive enonic fragment in **A** and **F**, opens a wide perspective for the synthesis of new organic compounds with expedited chelating properties.

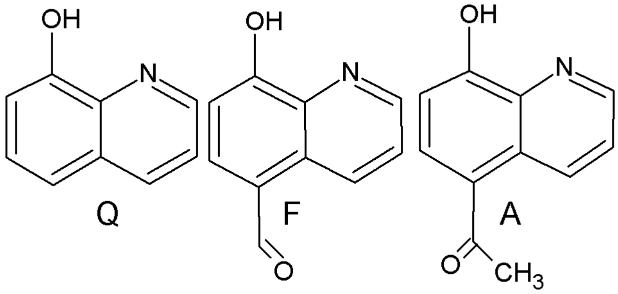


Figure 1. *Structures of chelating agents (ACD/ChemSketch)*

There are no known applications of **A** and **F** as chelating agents for any type of titration although many derivatives have been used as chelating agents (Amish *et al.*, 2012). Traditionally, titrations of metals by complexation reactions are performed using ethylenediaminotetraacetic acid (EDTA) when metal concentrations are 0.001 mol/L or higher. These titrations have the advantage that EDTA has little environmental impact and low cost, and is easy to handle and stable. In addition, EDTA-metal reactions are rapid, quantitative and stoichiometric, and their formation constants are generally large which produce very sharp titration curves. However, EDTA is not selective (titrations determine the total concentration of the metals in solution), and typically cannot titrate metal concentrations lower than 0.001 mol/L. Furthermore, most indicators are unstable, several of them bond irreversibly to metals so they should be back-titrated, (Skoog *et al.*, 2006) and have unclear color changes.

For these reasons, other methods as electrochemical or spectrophotometric techniques are used for endpoint detection which allow a decrease in detection limits and titration of environmental samples where metal concentration is lower. Additionally, selective chelating agents have been developed for certain metals; **Q** has been used as a chelating agent for divalent transition metals (Ahmed *et al.*, 1998). This area of analytical chemistry continues attracting interest and many metals are still determined using various chelating agents (Dapporto *et al.*, 2000; Ambrosi *et al.*, 2007; Ambrosi *et al.*, 2009). For example, Th^{4+} has been titrated using bromocresol orange (BCO)-cetylpyridinium bromide (CPB) as indicator in a concentration range of 0.02-2.6 mg L^{-1}. The color of the ternary complex Th:BCO:CPB was used for the selective determination of Th^{4+} in the presence of many transition metals and a pK_f of 12.0 was found with the indicator and a molar absorptivity, ε, of 9.2 x 10^4 L mol^{-1} cm^{-1} at 560 nm (Khalifa and Hafez, 1998). In other experiments, **Q** was anchored on silica gel using **F** as reagent; modified silica was applied to metal preconcentration and determination by flame atomic absorption spectrometry (Goswami *et al.*, 2003).

We studied the compounds **A** and **F** as chelating agents for metal complexometric titrations with spectrophotometric end point detection and determined their dissociation constants and formation constants with Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+}.

MATERIALS AND METHODS

2.1 Synthesis of A and F

We prepared **A** and **F** from **Q** and identified them by ^1H NMR, IR, melting temperature, and elemental analysis (Marrugo-González *et al.*, 2012).

2.2 Method validation and pH effect

Optimum conditions were sought for the experiments, including pH and absorption wavelengths for metal-ligand complexes of **Q**, **A** and **F**, where metals and free ligands did not absorb. Titration curves with spectrophotometric endpoint have linear portions that are extrapolated to obtain the stoichiometric endpoint. The absorbance was corrected for the dilution that involves addition of titrant. This was done by multiplying the absorbance by the factor (V + v)/V, where V is the original sample volume and v is the total volume of analyte added when absorbance was measured. To determine the concentration of solutions of **Q**, **A** and **F**, these solutions were titrated (2.00 ml) with a standard solution of Fe^{3+} using a 250-μl syringe unless otherwise specified. Titrations were conducted in the spectrophotometer cells to avoid losses or contamination by transfers between containers. Stirring was achieved with a magnetic stirrer and the introduction of a small magnet cut to size into the cell.

A parameter of our complexometric titrations was pH; the sharpness of the spectrophotometric end point is expected to increase with pH when using acid-base chelating agents such as **Q**, **A** and **F**. Metal titrations were performed at pH values of 2, 4, 6, 8 and 10 using a 250-μl syringe to evaluate the effect of protonation extent of **A** and **F** in the sharpness of the end point. The solutions were buffered using alcoholic solutions of chloroacetic acid-sodium chloroacetate (pH 2), acetic acid-sodium acetate (pH 4 and 6), and ammonia-ammonium chloride (pH 8 and 10).

2.3 Dissociation Constants

The dissociation constants of **Q**, **A** and **F** were obtained by measuring the pH values of solutions of these compounds during potentiometric titrations with NaOH using a glass electrode, prior to the corresponding equivalence point by the Bjerrum ñ (n-bar) method (Billo, 2001), Solutions of **Q**, **A** and **F** in ethanol (5.00 ml 0.0100 mol/L) were diluted with ethanol (to 25.00 ml). These solutions (2.00 ml) were titrated with 0.100M NaOH. Before titrations, HCl (10.00 ml 0.0100 mol/L) was added to **Q**, **A** and **F** solutions to acidify. All solutions were prepared and diluted in ethanol.

2.4 Formation Constants

Total formation constants were obtained using Bjerrum´s method, which is based on the competition of a metal with the ligand protons at low pH. In this method, the formation constant, Kf, corresponding to the equilibrium $M^{n+} + xL <=> ML_x^{n+}$, is calculated:

$$Kf = \frac{[ML_x^{n+}]}{[M^{n+}][L]^x}$$

ML_x^{n+} concentration was calculated from the absorbance, A, and the molar absorptivity, ε through the Beer-Lambert equation, $A = [ML_x^{n+}]\varepsilon b$, where b is the length of the cell, 1 cm; $[M^{n+}]$, the free metal concentration, is the initial metal concentration minus the ML_x^{n+} concentration. [L'], the concentration of all species of L (L^-, L, L^+), is the initial concentration of L minus $x[ML_x^{n+}]$. The concentration of free ligand, L, was calculated with α, the molar fraction: $\alpha = [L]/[L']$; α was calculated with the pH values of solutions of L and its pKa. In Bjerrum´s method several solutions are prepared with identical concentrations of the same metal and ligand at different acid pH values; then, pH and the absorbance of these solutions are measured. In our study, we prepared solutions of **Q**, **A** and **F** (25.00 ml $2.00x10^{-3}$ mol/L or lower) in ethanol and pH was changed by adding NaOH or HCl. The molar absorptivity was measured in an independent experiment at pH> 10 (Billo, 2001), at which most ligand was deprotonated and formed the major amount of the complex. The stoichiometry of complexes was determined by spectrophotometric titrations.

2.5 Materials, Instruments and Reagents

Standard solutions of Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+} were prepared from 1000.0 ppm stock solutions (Merck and MolLabs). The synthesis of **A** and **F** has been reported (Marrugo-González *et al.*, 2012). For titrations, An UV S2100+ Cole Parmer spectrophotometer and an Orion 940 potentiometer with a glass electrode were used. For accuracy, pH values were recorded when drift was less than ±1 mV per minute much less than that suggested by the manual instructions (<±3 mV per minute). The potentiometer was calibrated with buffer solutions of pH 2, 4, 7 and 10.

RESULTS AND DISCUSSION

Q was used to compare its properties with those of its derivatives **A** and **F**. We compared the acid dissociation constants of **Q**, **A** and **F** and their formation constants with transition metals.

3.1 Determination of the concentration of Q, A and F solutions

These concentrations were determined by spectrophotometric titrations with standard Fe^{3+} solutions. Figure 2b shows the endpoint of a titration curve of **F** with Fe^{3+}, the intersection of the linear portions extrapolations. These results were confirmed by acid-base titration of **Q**, **A** and **F** solutions.

3.2 Spectrophotometric titrations with Q

Figure 3 shows the UV-visible spectra of 1.00×10^{-4} mol/L solutions of **Q**, Pb^{2+}, and PbQ_2^{2+} at pH 4. Pb^{2+} solutions was titrated between 360 and 380 nm because the peak of PbQ_2^{2+} at this wavelength did not overlap with the peaks of **Q**, ethanol, or Pb^{2+}. In this way, the wavelengths to titrate **Q**, **A** and **F** solutions with other metals were found. Figures 4 and 5 show the corresponding spectra for Fe^{3+} at different pH values.

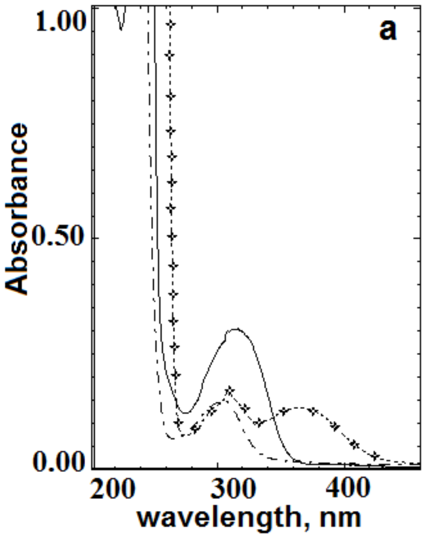


Figure 3. *UV-visible spectra of 1.00×10^{-4} mol/L solutions of **Q** (—), Pb^{2+} (– - –), and PbQ_2^{2+} (✧) at pH 4 (a). **Q** solutions were titrated with Pb^{2+} at 370 nm where the metal complex absorbed but not **Q**; the spectra of **Q** and Pb^{2+} did not interfere, nor that of ethanol.*

3.3 Spectrophotometric titrations with F

Figure 4 shows the UV-visible spectra of **F**, Fe^{3+} and $Fe(F)_3^{3+}$ solutions at pH 2, 4, 6, 8 and 10. At 600 nm, only $Fe(F)_3^{3+}$ absorbed but not Fe^{3+} or **F** therefore titrations of **F** with Fe^{3+} were performed at this wavelength. Moreover, the sharper end point allows **F** to be better titrated with Fe^{3+} at pH 6 as explained in the discussion of Figure 6.

3.4 Spectrophotometric titrations with A

Figure 5 shows the UV-visible spectra of **A**, Fe^{3+}, and $Fe(A)_3^{3+}$ at pH 2, 6, 8, and 10. At 600 nm, only $Fe(A)_3^{3+}$ absorbed but not Fe^{3+} nor **A** so that the titration of **A** with Fe^{3+} was performed at 600 nm. Also, the titration of **A** with Fe^{3+} was better at pH 6 for the sharper end point as explained in the discussion of Figure 6.

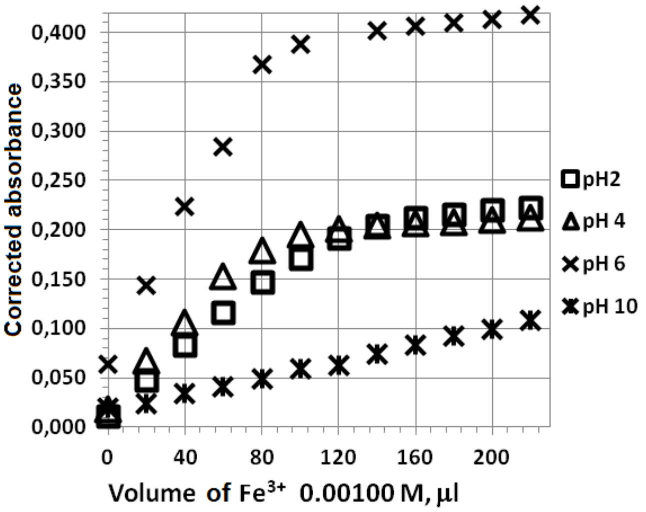


Figure 6. *Effect of pH on the potentiometric titration of 1.2×10^{-3} mol/L solutions of **A** with Fe^{3+} 0.00100 mol/L in ethanol. The absorbance increased up to pH 6 and then decreased, probably because at acidic pH, **A** was not fully deprotonated and at alkaline pH, Fe^{3+} precipitated as hydroxide. The best pH for titration was 6.*

Figure 6 shows the effect of pH on the shape of the titration curves of **A** with Fe^{3+} in ethanol. The absorbance of the product, $Fe(A)_3^{3+}$, increased up to pH 6 and then decreased at higher pH values, probably due to a combination of two antagonistic factors: at acidic pH values, complexing of Fe^{3+} with **A** was incomplete because deprotonation is low and at alkaline pH values Fe^{3+} precipitated as hydroxide and did not allow a proper observation of the endpoint. The best pH for titration of **A** with Fe^{3+} was 6, because the change in absorbance and the inflection at the end point were larger than at other pH values due to a balance of the two factors mentioned above. These results were consistent with the findings of Moeller (1943) who found that Fe^{3+}, Cu^{2+}, and other metal ions were not extracted at very acidic or very alkaline pH values but intermediate ones (Moeller, 1943). In this way, wavelengths and pH values for titrations of **F** with metals were selected.

3.5 Molar absorptivities

Table 1. Molar absorptivities, ε, (x10^4) in L cm^{-1} mol^{-1} for the absorption peaks of Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+} complexes with **Q**, **A** and **F** in ethanol. Wavelengths in nm at which measurements were made appear in brackets. Measurements were made saturating **Q**, **A** and **F** with metal so that complex concentration was stoichiometric.

Metal	**ε, (x10^4) in L cm^{-1} mol^{-1}**		
	Q	**A**	**F**
Fe^{3+}	0.87(380)	2.4(366)	2.2(380)
Cu^{2+}	0.48(382)	1.8(380)	1.9(400)
Zn^{2+}	0.47(375)	1.2(395)	0.78(380)
Pb^{2+}	0.78(380)	2.6(380)	1.4(380)

Table 1 shows the molar absorptivities (ε) for the absorption peaks of Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+} complexes with **Q**, **A** and **F** in ethanol. Molar absorptivities were measured at pH> 10 where the ligands were considered to be completely deprotonated and the maximum amount of the complex was formed so that the maximum absorbance occurred. ε_{max} was measured at various pH values up to pH> 10 to verify that the maximum absorbance was obtained and was not measured at pH values where the ligands were still protonated. ε_{max} values of 2.4x10^3 for **Q** (316 nm), 4.7x10^3 for CuQ_2^{2+} (410 nm), and 4.4x10^3 for ZnQ_2^{2+} (402 nm) in dimethylsulfoxide have been reported (Monzon *et al.*, 2011). Due to complex formation, there is an increase of ε_{max} and shift to longer wavelengths in these values when passing from **Q** to CuQ_2^{2+} and ZnQ_2^{2+}. Because of the large values (>10^4 L cm^{-1} mol^{-1}), those large ε_{max} values may correspond to charge transfer transitions (Skoog *et al.*, 2006). Wavelengths reported in Table 1 are those used to measure the absorbances to calculate the formation constants (Table 2).

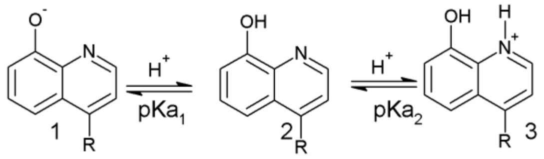
Table 2. Total formation constants (expressed as pK_f) of **A** and **F** complexes with Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+} (four upper rows) and dissociation constants (expressed as pKa, two lower rows) of **Q**, **A** and **F**, in ethanol. The calculations used absorbances measured at the wavelengths reported in Table 1. The pKf values are the average of at least three different experiments.

Ion/pK_a	**Ligand**		
	Q	**A**	**F**
Fe^{+3}	37.8±0.2, 33.9 [A,B]	31±2	32±1
Cu^{+2}	23.7± 0.1, 13.1 [A,B]	22.5±0.7	27.1±0.2
Zn^{+2}	23.3±0.3, 9.36 [A,B]	21.4±0.1	26.2±0.3
Pb^{+2}	22.4±0.1, 9.30 [A,B]	21.2±0.2	24.9±0.4
pK_{a1}	5.3±0.2, 5.06 [C,D] 4.88,[E] 4.91 [F]	4.8±0.2	2.9±0.8 3.97 [G]
pK_{a2}	10.0±0.4, 9.81 [C, D] 9.81 [F]	9.6±0.2	9.5±0.1 11.54 [G]

[A] calculated in 50% dioxane-water; [B] Johnston and Freiser, 1952; [C] Perrin, 1983 (from reference 20); [D] Tsakovski *et al.*, 2002; [E] Irving *et al.*, 1949; [F] Dean, 1999; [G] Takamoto, *et al.*, 1965.

3.6 Dissociation Constants

Acid dissociation constants of **A** and **F** in ethanol are shown in Table 2. Compounds **Q**, **A** and **F** are amphiprotic: they contain a weakly basic pyridine nitrogen and a weakly acidic phenolic group. The species of **A** and **F** which predominate in solution are: RQ^- (basic medium, **1**), RHQ (neutral medium, **2**) and RH_2Q^+ (acid medium, **3**), where R can be H, or acetyl or formyl groups, and **Q** is the 8-hydroxyquinolinic fragment:



Deprotonation reactions of **Q**, **A** and **F** (ACD/ChemSketch version 12).

The first hydrogen that is lost during an acid-base titration of **Q** or its derivatives is bonded to the nitrogen and the second one is that of the hydroxyl group in the ring. Therefore, these compounds should show two endpoints. These hydrogens in **A** and **F** were more acidic than those of **Q** due to the inductive effects of the acetyl and formyl electronegative substituents at position 5 in **A** and **F** that attract electrons from the hydroxyquinolinic ring. In turn, **F** was more acid than **A** because the methyl in the acetyl group provides electrons to the carbonyl group decreasing electron withdrawing from the hydroxyquinolinic ring, a phenomenon similar to that explained before (Tsakovski *et al.*, 2002).

Average dissociation constants in aqueous solution for **Q** reported in the literature were pK_{a1} = 5.06 (hydrogen in the pyridine nitrogen) and pK_{a2} = 9.81 (hydroxyl group) (Tsakovski *et al.*, 2002). In non-aqueous solvents with dielectric constant, D, less than that of water (D = 78.5) such as ethanol (D = 24), **Q** is less acidic because the formation of ions is hindered. The dissociation constants in Table 2 were those expected based on the inductive effect and solvent influence on the proton acidity: the pKa values of **F** (9.5 and 2.9) were lower than those of **A** (9.6 and 4.8). These, in turn, were lower than those reported for **Q** in aqueous solution (9.81 and 5.06) (Tsakovski *et al.*, 2002), and the latter were also smaller than those obtained in our work for **Q** in ethanol (10.0 and 5.3) where lower acidity was expected for these hydrogens than in aqueous solutions.

3.7 Formation constants

The formation constants of Fe^{3+}, Cu^{2+}, Zn^{2+}, and Pb^{2+} with **Q**, **A** and **F** in ethanol (Table 2) were determined by Bjerrum´s method (Billo, 2001). Compounds **A** and **F** formed complexes with large formation constants with divalent and trivalent metals, suitable to titrate metal ion solutions with spectrophotometric endpoint. The stability of metal complexes with **A** and **F** could be explained by their highly basic functional groups. The sequence of complex stability for various divalent metals with a ligand has been shown to be rather inflexible regardless of the ligand used. The order of stability of metal complexes with **Q**, **A** and **F** in ethanol was $Fe^{3+} > Cu^{2+} > Zn^{2+} > Pb^{2+}$ which was consistent with previous findings Johnston and Freiser, 1952) and the Irving-Williams series (Irving and Williams, 1953). Stability constants followed the order **A** < **F**, which was expected from the acidity of the pyridinic and phenolic hydrogens in **A** and **F**.

Table 2 also shows that as the ion charge increased, in the case of Fe^{3+}, the value of the complex formation constant increased due to the larger metal-ligand attraction so the sharpness of the spectrophotometric endpoint also increased, which agrees with the literature (Irving and Williams, 1953). The structure of complexes metal-hydroxyquinoline (MeQ_2^{2+}), that should be similar to the complexed formed by **A** and **F**, has been reported as square planar or tetrahedral (Nicolau and Yoshikawa, 1998).

CONCLUSIONS

In general, **A** and **F** resulted excellent chelating agents for complexometric titrations with large formation constants of metal complexes, especially with Fe^{3+}. Increasing the pH values increased the spectrophotometric endpoint sharpness due to increasing deprotonation of these ligands at alkaline pH which would leave more pairs of free electrons to bond with the metals. However, above certain pH values, endpoint sharpness decreased, possibly due to precipitation of metals as hydroxides. The stability order of metal complexes with **Q**, **A** and **F** in ethanol was $Fe^{3+} > Cu^{2+} > Zn^{2+} > Pb^{2+}$ as the Irving-Williams series. Some issues remain as the large formation constant of FeQ_3^{3+}, and the formation constants for **A** with metals, lower than those for **Q**, which did not agree with the fact that hydrogens in **A** were more acidic than those of **Q**. Because of their large formation constants, these compounds can find potential applications in masking, preconcentration, and titration of metals by complexation and oxidation-reduction reactions.

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SUPPLEMENTARY MATERIAL

α values (distribution profiles) for different pH values for compounds Q, A and F.

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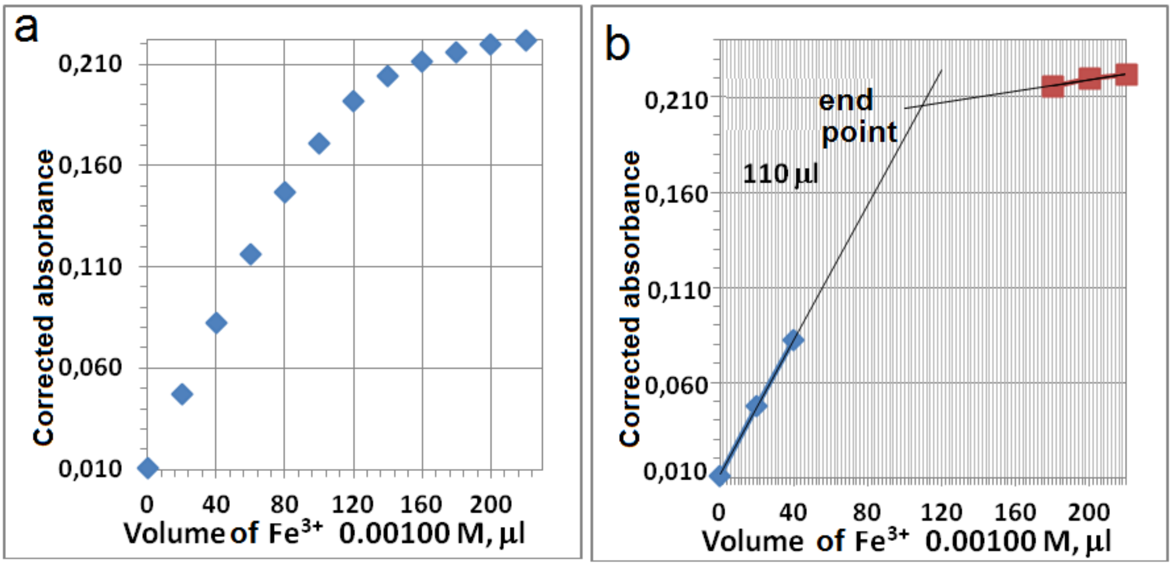


***Figure 2**. (a) Potentiometric titration curve of a 1.00x10^{-4} mol/L solution of **F** with Fe^{3+} 1.00x10^{-3} mol/L at pH 2 and 600 nm. (b) The volume at the end point is the intersection of the linear portions of the titration curve.*

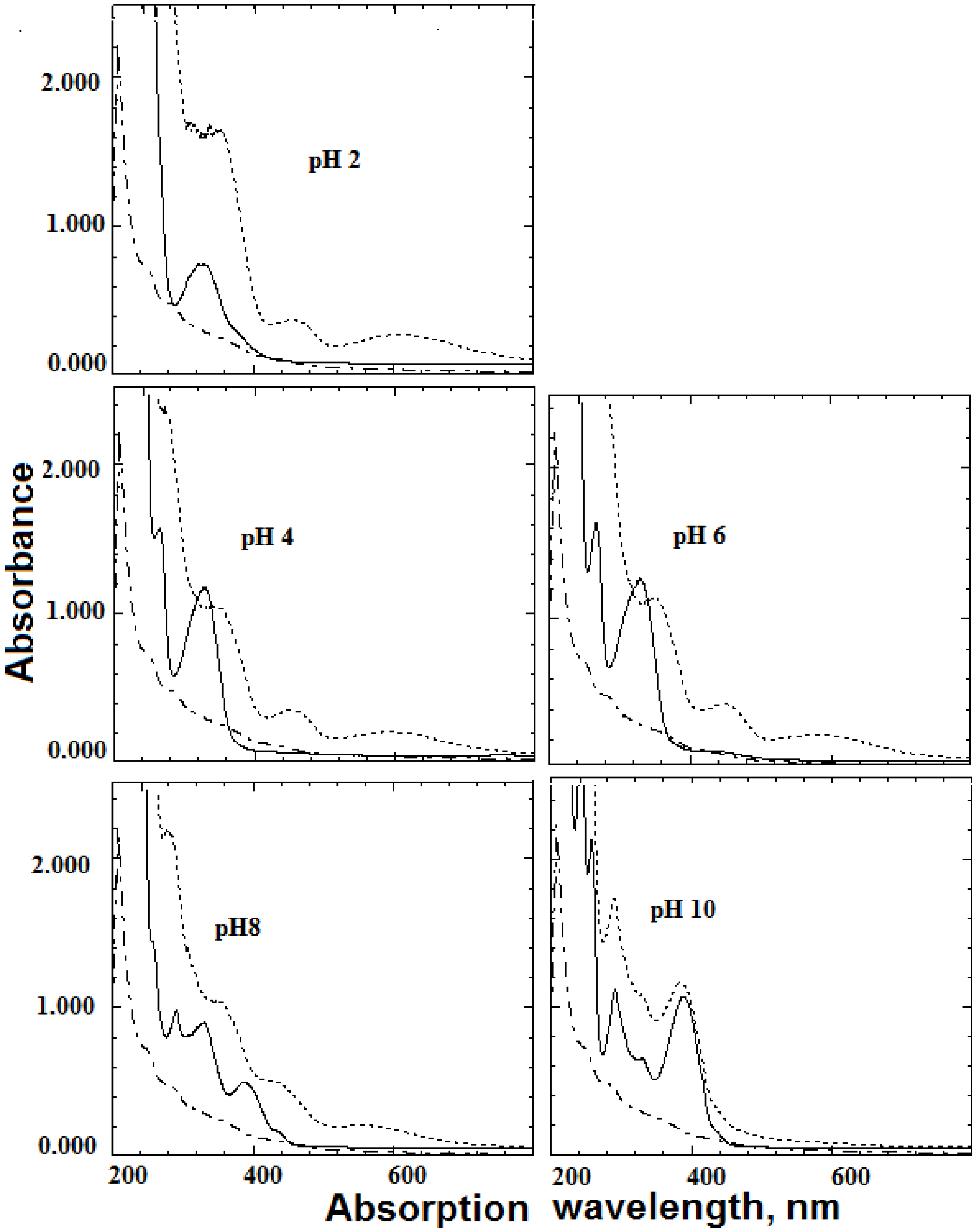


Figure 4. *UV-visible spectra of* ***F*** *(—),* Fe^{3+} *(– - –) and* $Fe(F)_3^{3+}$ *(---) solutions at different pH values. Solutions of* ***F*** *were titrated with* Fe^{3+} *at pH 6 and 600 nm where the metal complex absorbed but not* ***F*** *nor the free metal.*

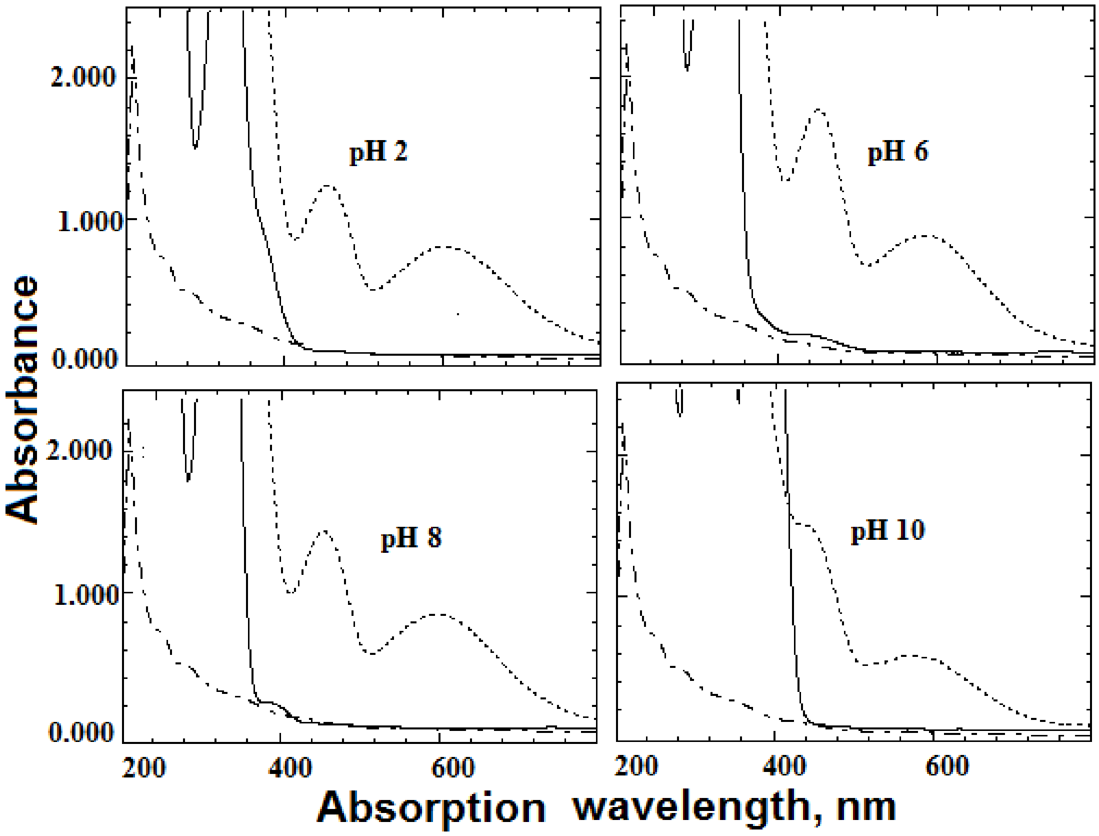
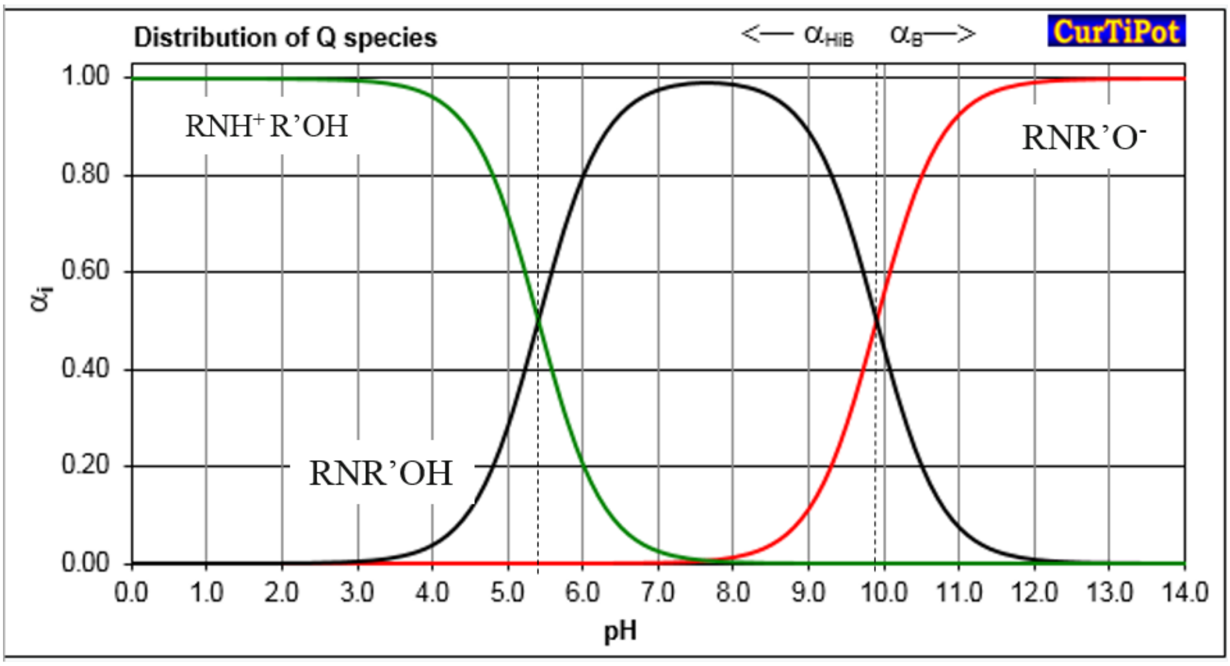


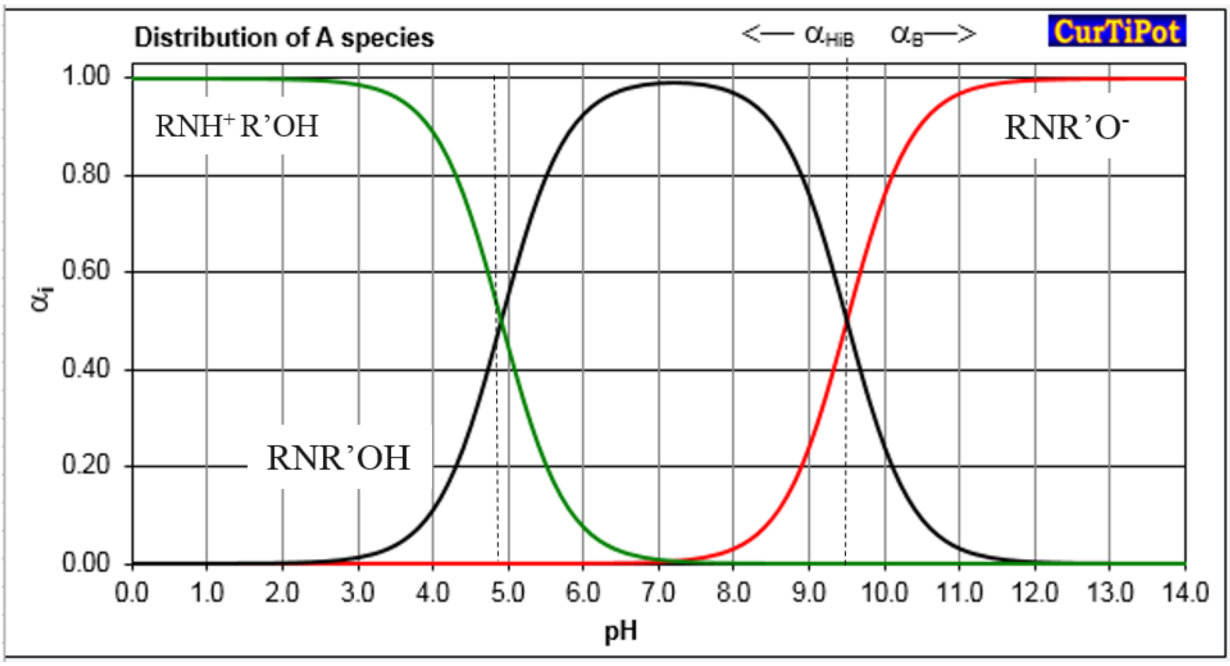
Figure 5. *UV-visible spectra of **A** (—), Fe^{3+} (– - –) and $Fe(A)_3^{3+}$ (---) solutions at different pH values. Solutions of A were better titrated with Fe^{3+} at pH 6 and 600 nm where the metal complex absorbed but not A nor the free metal.*

ELECTRONIC SUPPLEMENTARY MATERIAL



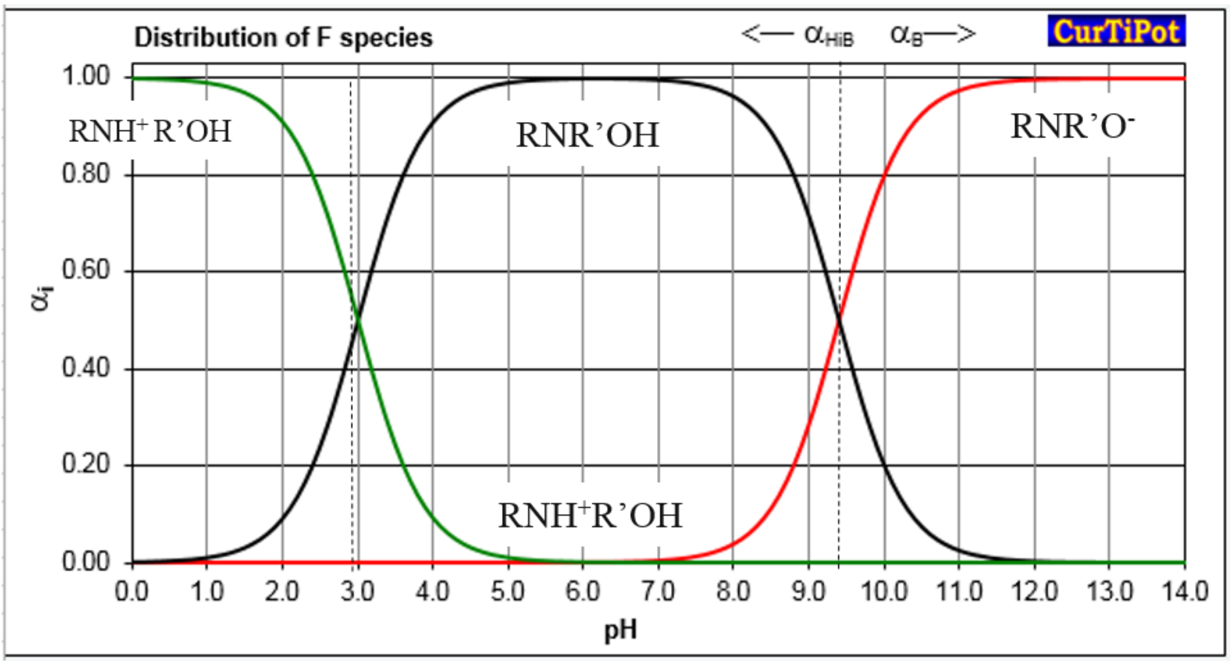
$RNH^+R'OH \Leftrightarrow RNR'OH \Leftrightarrow RNR'NO^-$

α values for different pH values for compound Q (Curtipot software www.iq.usp.br/gutz/Curtipot.html). RNH^+ R'OH is 8-hydroxyquinoline protonated at the nitrogen; RNR'OH is the neutral molecule and $RNR'O^-$ is 8-hydroxyquinoline deprotonated at the OH group.



$RNH^{+}R'OH \Leftrightarrow RNR'OH \Leftrightarrow RNR'NO^{-}$

α values for different pH values for compound A (Curtipot software www.iq.usp.br/gutz/Curtipot.html). RNH^{+} R'OH is 5-acetyl-8-hydroxyquinoline protonated at the nitrogen; RNR'OH is the neutral molecule and $RNR'O^{-}$ is 5-acetyl-8-hydroxyquinoline deprotonated at the OH group.



$RNH^{+}R'OH \Leftrightarrow RNR'OH \Leftrightarrow RNR'NO^{-}$

α values for different pH values for compound F (Curtipot software www.iq.usp.br/gutz/Curtipot.html). RNH^{+} R'OH is 5-formyl-8-hydroxyquinoline protonated at the nitrogen; RNR'OH is the neutral molecule and $RNR'O^{-}$ is 5-formyl-8-hydroxyquinoline deprotonated at the OH group.