

Equilibrium Constants of the Fe(III)–Dopamine System in Aqueous Solution

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The system Fe(III)–Dopamine was investigated potentiometrically in aqueous solution and equilibrium constants were evaluated for the resulting complexes by means of a fitting procedure. The existence of hydroxy complexes is hypothesized which is consistent with the results of a previous EPR and NMR investigation.

Introduction

A number of investigations into the interaction of different metal ions with catecholamines in aqueous solution has been reported, because of their possible involvement in neuronal activity [1–2]. Some of these studies were carried out potentiometrically and spectrophotometrically providing information on the stoichiometry of the complexes with divalent metal ions and their formation constants [3–12], while NMR spectroscopy furnished detailed knowledge of their mutual interactions [13, 14].

The more complex chemistry of Fe³⁺ in aqueous solution [15, 16] prevented any rationalization of potentiometric data since, contrary to the divalent ions, inflections at non integral values of equivalents of added base were observed, which were attributed either to the occurrence of oxidation of the catecholamines or to the formation of polynuclear species [3].

Different behaviour between Fe³⁺ and other divalent metal ions in binding Dopamine was also shown by means of NMR and EPR spectroscopy [17].

To gain a better insight into this subject we performed a potentiometric investigation on the Fe³⁺–Dopamine system in aqueous solution.

Experimental

Material and Methods

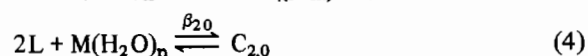
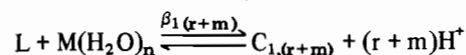
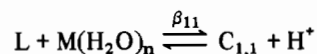
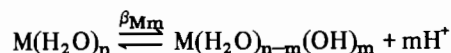
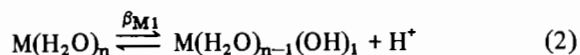
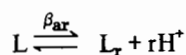
Dopamine hydrochloride (DA), NaOH, Fe(NO₃)₃·9H₂O, KNO₃ were Merck products.

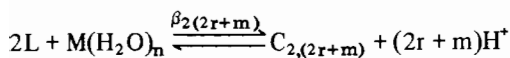
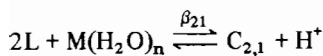
Five different titrations with NaOH 0.1 M of the Fe³⁺–DA system were performed; the DA concentration was kept at 3 × 10^{−3} mol/l while the Fe³⁺ concentration ranged from 3 × 10^{−3} to 3 × 10^{−4} mol/l. 50 ml of the solution of Fe³⁺–DA were titrated at 20 °C under nitrogen atmosphere to prevent DA oxidation at a constant ionic strength, obtained by means of KNO₃ 1 M.

The collection of NMR and EPR data has been described elsewhere [17b].

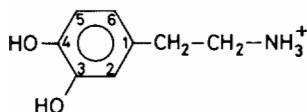
Calculations

If one assumes that a ligand, L, and a metal ion, M, form complexes of 1:1 and 2:1 stoichiometry with different degrees of deprotonation, the system can be described by the following equations:





Here the ligand corresponds to the completely protonated form of DA:



and the β_a 's represent the overall acidity constants of the ligand, while the β_M 's refer to the loss of the protons from the hydrated metal ion; r is the number of the acidic protons of the ligand and m the corresponding value for the hydrated metal ion. Equations (3) and (4) describe the formation of the complexes $C_{i,j}$ from the completely protonated reagents: the first subscript indicates the stoichiometry of the complex (1:1 or 2:1) and the second one the degree of deprotonation of the complexes, the limiting values being $(r+m)$ for the 1:1 species and $(2r+m)$ for the 2:1 species.

The experimental data were analysed with a BASIC program on a HP-85 graphic computer.

β_a 's and β_M 's being known (from the literature or by potentiometric measurements), the program optimizes the initial estimates of β_{ij} 's by the Gauss-Newton [18-21] non linear least squares procedure. This method minimizes

$$\chi^2 = \sum_1^N (T_i^e - T_i^c)^2,$$

where T_i^c and T_i^e are the i th calculated and experimental values of the ratio of the mol of the titrant used to the total mol of the ligand, for a given pH value, and N is the number of experimental points, to which unit weights were assigned.

The best fitting procedure is iterative and stops after a prefixed number of cycles or when the χ^2 relative difference between two consecutive cycles is less than a given value. A damping factor of 0.2 for the correction term of the parameters was used, which, although it lengthens the calculation time, ensures convergence of the fitting procedure. The program also allows the calculation of the standard deviations of the parameters from the diagonal elements of the variance-covariance matrix.

Results and Discussion

Some of the titration curves for the Fe^{3+} -DA system are reproduced in Fig. 1: comparison with the free ligand titration curve and the appearance of

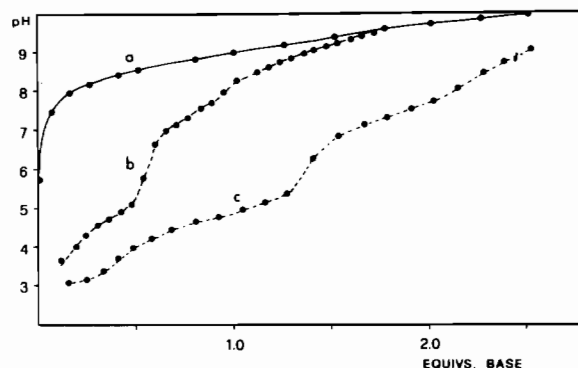


Fig. 1. Titration curves (pH vs. the ratio (mol of titrant used/mol of ligand) of (a) DA 3×10^{-3} M, (b) DA 3×10^{-3} M in the presence of Fe^{3+} 6×10^{-4} M, (c) DA 3×10^{-3} M in the presence of Fe^{3+} 1.5×10^{-3} M. The dotted lines are the calculated curves.

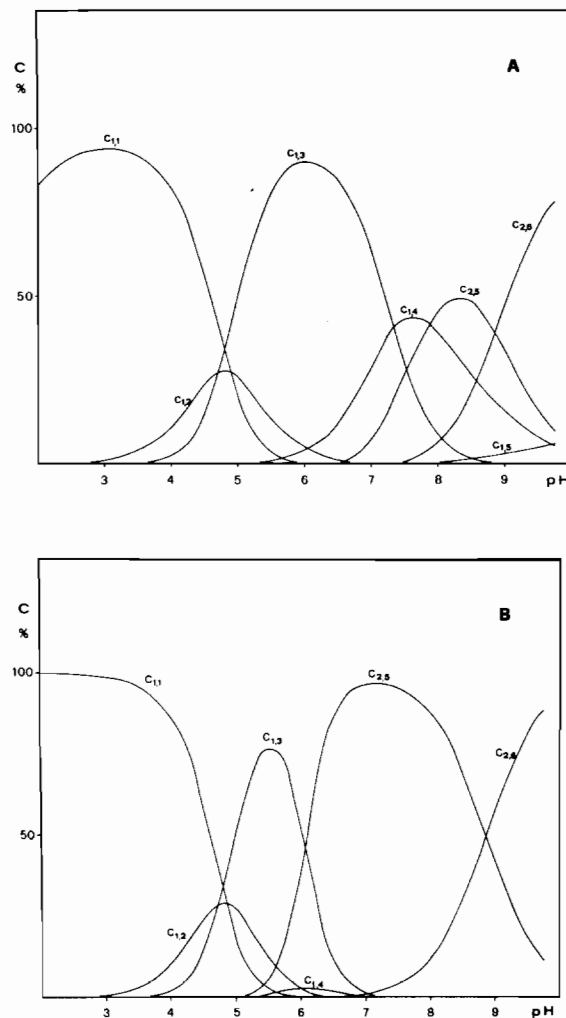


Fig. 2. pH dependence of the concentration distribution of the various complex species calculated for Fe^{3+} -DA system: (A) DA 3×10^{-3} M, Fe^{3+} 1.5×10^{-3} M; (B) DA 1 M, Fe^{3+} 5×10^{-3} M.

TABLE I. Cumulative Stability Constants and Standard Deviations of Fe³⁺ Complexes with Dopamine at 20 °C. Ionic Strength = 1 M (KNO₃).

Complex	pβ _{ij}
C ₁₁	-1.50 ± 0.09
C ₁₂	3.4 ± 0.2
C ₁₃	7.96 ± 0.08
C ₁₄	15.3 ± 0.1
C ₁₅	24.3 ± 0.4
C ₂₅	19.96 ± 0.09
C ₂₆	29.0 ± 0.1

The same constants can be expressed in the usual notation if we consider the deprotonated form of the ligand L' = β_{a3}L/H³. Therefore

C ₁₁ = ML'H ₂	β ₁₁₂ = ML'H ₂ /(M L' H ⁺ ²) = β ₁₁ /β _{a3}
C ₁₂ = ML'H	β ₁₁₁ = ML'H /(M L' H ⁺) = β ₁₂ /β _{a3}
C ₁₃ = ML'	β ₁₁₀ = ML' /(M L') = β ₁₃ /β _{a3}
C ₁₄ = ML'(OH)	β ₁₁₋₁ = ML'(OH) /(M L' H ⁺ ⁻¹ K _w) = β ₁₄ /(β _{a3} K _w)
C ₁₅ = ML'(OH) ₂	β ₁₁₋₂ = ML'(OH) ₂ /(M L' H ⁺ ⁻² K _w ²) = β ₁₅ /(β _{a3} K _w ²)
C ₂₅ = ML' ₂ H	β ₁₂₁ = ML' ₂ H /(M L' ² H ⁺) = β ₂₅ /β _{a3} ²
C ₂₆ = ML' ₂	β ₁₂₀ = ML' ₂ /(M L' ²) = β ₂₆ /β _{a3} ²

the overall trends are indicative of both a strong interaction between the reagents and the occurrence of at least three different complexes. The latter finding is substantiated by a drastic change of the solution's colour (from green to blue and finally red) corresponding to the curve's inflections. The fitting procedure to the experimental data was performed, in a first approach, by taking into consideration the various deprotonated species of the 1:1 complex C_{1,j}. The β's of the ligand and the aquo-metal-ion, averaged on the available literature data, are: pβ_{M1} = 2.75, pβ_{M2} = 6.99 [22–26], pβ_{al} = 8.93, pβ_{a2} = 19.38 and pβ_{a3} = 31.53 [12, 27]. Within this approximation the experimental trends were correctly reproduced up to the second inflection point of the titration curve while a failure in the fitting procedure was observed beyond this point. The agreement between the calculated and experimental data greatly improved on introduction of the C_{2,j} complexes. The final sum of the squared residuals χ² was found to range from 0.009 to 0.016. Table I lists the final set of the optimized constants and the corresponding standard deviations; the good quality of the agreement is also visualized in Fig. 1 where the calculated curve and the experimental points are compared.

Figure 2A shows the pH dependence of the concentration distributions for the various complexes. Of the two main species C_{1,1} and C_{1,3}, the former probably occurs by deprotonation of one of the phenolic hydroxy groups, while the latter arises from

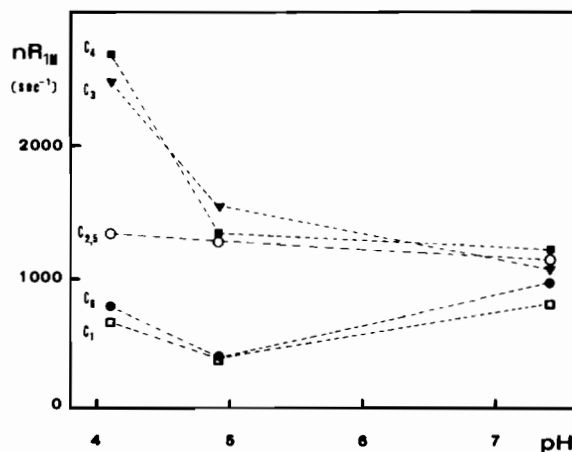


Fig. 3. C-13 spin–lattice relaxation rates of DA (1 M) in presence of Fe³⁺ (5 × 10⁻³ M) at variable pH; see text for the numbering of carbon atoms. R_{1M} represents the nuclear dipole–electron dipole interaction of the DA–Fe³⁺ complexes; n is the number of ligand molecules per metal ion).

the full deprotonation of the catecholic function together with the release of one proton from the coordinated water molecules rather than from the terminal NH₃⁺ group. This assumption is supported by:

i) the results of a previous NMR investigation [17] which excluded the direct involvement of the aminic group in binding Fe³⁺;

ii) the comparison of the pK's of the first and second deprotonation of $\text{Fe}(\text{H}_2\text{O})_6^{3+}$ with that of $-\text{NH}_3^+$ in DA.

As to the complexes with a 2:1 stoichiometry, two species $\text{C}_{2,5}$ and $\text{C}_{2,6}$ are found to occur in the examined pH range. These species originate from the full deprotonation of two catechols (4 protons) together with the release of one proton from the hydration water molecules. As far as the complex $\text{C}_{2,6}$ is concerned, it is reasonable to assume that the sixth deprotonation occurs in the ammonium group since the pK_a of this function falls in the pH range of existence of $\text{C}_{2,6}$.

Figure 2B illustrates the pH dependence of the concentration distributions when the reagents' concentrations become comparable to those used in a previous NMR and EPR study [17b]. Three dominant species are seen to occur with stoichiometries 1:1, 1:1 and 2:1, the latter two arising from the deprotonation of a water molecule. The EPR spectra at variable pH showed a broadening of the signals up to $\text{pH} = 5$, beyond which disappearance of the spectrum was observed. These findings, which were interpreted in terms of the shortening of the Fe^{3+} electronic relaxation time, can be attributed, in the light of the results here reported, either to the formation of hydroxy complexes or to the chelation process by the catechol group, rather than to a change of the stoichiometry. This result is paralleled by the change of the C-13 paramagnetic relaxation rates of DA (Fig. 3) at pH's 4 and 5. Beyond this latter value the change in the relaxation rates can be accounted for, on consideration of the curves in Fig. 2B, also by the varied stoichiometry of the complexes.

Acknowledgement

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