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Research paper

Di- and tetranuclear gadolinium (III) complexes of 2-hydroxypropane-1,2,3-tricarboxylic acid and 1,2,2-trimethylcyclopentane-1,3-dicarboxylic acid : identification and characterization

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Abstract

Our studying involved, Identification and characterization of two novel gadolinium complexes with 2-hydroxypropane-1,2,3-tricarboxylic acid (citric acid) noted H_3L and 1,2,2-trimethylcyclopentane-1, 3-dicarboxylic acid (camphoric acid) noted H_2L in aqueous solution and in pH range 5,5–7,5. These acids containing the donor atoms (oxygen of OH and COOH), the formatted complexes are colorless and have no absorption band UV–visible. So, to determine the composition and stabilities of these complexes in solution, we have used an analytical technique called «Indirect Photometry Detection (IPD) » have identified multi-nuclear and multi-dentate complexes studied in this work. Giving for these colorless complexes with a mole ratio (M:L): (4:2) for Gd (III)–Citric acid and (2:2) Gd (III)–Camphoric acid. In addition, we have shown that the compositions and stabilities constant of these complexes are depended on the acidity of the medium.

Keywords: *Citric and Camphoric Acid; Coloress Complexes; Indirect Photometry Detection; Gadolinium Complexes; Stability of Contrast Agents.*

1. Introduction

The gadolinium ion is highly toxic in its hydrated form $[Gd(H_2O)_8]^{3+}$, Its complexation with an organic ligand reduces this toxicity for IRM or other medical using. This complexation should be administered in the form thermodynamically stable (Reimer et al. 1996 p.36). The solution consists of enclosing the gadolinium ion Gd(III) in the organic ligands to form Gd–Ligands complexes non toxic and very stable in the human body (Thunus & L, Lejeune 1999 p.125, Guo-Ping et al. 2005 p 11, Yoshimasa et al. 2016 p. 148, Sofía & Martín 2017 p. 31). The most widely ligands used are polyaminocarboxylates and their derivatives. In this work, we have studied the formation of colorless gadolinium complexes with some linear ligands in dilute solutions (citric and camphoric acid). To study of these colorless complexes, we developed a new analytical technique for determining the compositions and stabilities of some colorless complexes, which have no absorption band UV–visible. This technique is the Indirect Photometry Detection (IPD), based on competitive reactions by ligand–ligand exchange.

$$Gd–L_n + n'L' \longleftrightarrow Gd–L'_{n'} + nL$$

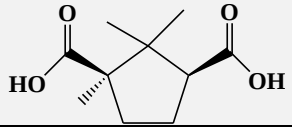
Color reagent Ligand Colorless Complex Auxiliary Ligand

This method is simple, reproducible, effective and applicable to very dilute solutions. Thus, the importance of IPD technique was also revealed by its adaptation to other techniques of separation, determination and characterization, such as liquid chromatography (Rocklin 1991 p. 175, Verchere &, Dona 1992 p. 437), capillary electrophoresis (Morin et al. 1994 p. 178), continuous flow analysis (FIA) (Ramshing et al. 1980 p. 165) and Ramn, IR, RMN spectroscopies (Hlaïbi et al. 2009 p. 310, Riri et al. 2014 p. 130). Some studies show that this technique is very effective for identifying some colorless gadolinium complexes (Riri et al. 2011 p. 303, Riri et al. 2013 p. 49) and tungstate complexes of sugars and organic ligands (Millan et al. 1995 p. 2334, Riri et al. 2014 p. 130). The detection or monitoring of certain diseases sometimes requires injection gadolinium complexes because of the interesting electronic and magnetic properties of this ion (Hiroyuki et al. 2002 p. 1119, Nonat et al. 2006 p. 7133). The most contrast agents used in MRI are complexes of amino acids and carboxylic acids with some lanthanides (Anelli et al. 1997 p. 125, Angela & Wing-Tak 2008 p. 1323). Currently, most contrast agents used in MRI are complexes of gadolinium–DTPA, gadolinium–BOPTA, gadolinium–DOTA (Anelli et al. 1997 p. 125, Angela & Wing-Tak 2008 p. 1323, Nwe et al. 2010 p. 5925, Moller & Sasu 2010 p. 125, Jonathan et al. 2010 p. 10056) and its analogs, which are modified to enhance the contrast effect on fabric (Tsan-Hwang et al. 2001 p. 3357, Moller et al. 2011 p. 140, Lee et al. 2011 p. 83). Other studies have shown that gadolinium complexes of coumarin-3-

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carboxylic acid (2-oxo-2H-chromene-3-carboxylic acid) and its derivatives have very important pharmacological properties (Kostova et al. 2007 p. 8, Yue et al. 2017 p. 5700). In this work, investigations by indirect photometry detection (IPD) were carried out to study the interaction of the trivalent gadolinium ions, with conjugate base of citric and camphoric acid, detecting the majority of colorless complexes formed in solution and determining their compositions and stabilities constant ($logK_{xyz}$). Other studies are interested to studying the stabilities of camphoric acid (Huijie et al. 2015 p. 135, Elisa et al. 2017p. 147) and citric acid (Xuefei et al. 2017 p. 103, Soo et al. 2017 in press) complexes with the formation of polymers or organometallic complexes. The acidity constants and semi developed form of citric and camphoric acid are noted in the Table 1 (Bjerrum 1958, Serjeant & Dempsey 1979).

Table 1: Some Characteristics of Acids Studied

Acid	Chemical formula	pKa_1	pKa_2	pKa3
Citric (H_3L)	$HOOC-CH_2-(HOOC)C(OH)-CH_2-COOH$	3.13	4.76	6.50
Camphoric (H_2L)		4.70	------	------

2. Experimental section

2.1. Chemicals

Citric acid, Camphoric acid, NaOH, HCl, Chrome Azurol S (H_4Ch), Gagoliunium nitrate ($Gd(NO_3)_3.6H_2O$) and other chemicals were commercial products (Aldrich, Prolabo,…) of the purest available and analytical grade, used as received.

2.2. Indirect photometric detection

Standard Helios γ UV–visible spectrometer controlled by Vision 32 software was used for spectrometric measurements, using quartz cells of optical path length $l = 1cm$. The absorption measurements have been performed at room temperature and at wavelength $\lambda_{max} = 545nm$. Stock solutions of Gd (III) nitrate and Chrome Azurol S, were prepared with concentrations respectively $10^{-2}M$ and $10^{-3}M$. In a typical experiment, a solution ($v = 50\ mL$) of the colored sacrificial complex ($Gd-H_4Ch$) was prepared ($[Gd^{3+}] / [H_4Ch] = 1.5$), using it as a buffer of MESH (0.1 M) [2-(N-morpholino) sulfonic ethane acid]. The initial solution also contained a calculated amount of 1 M (NaOH) in order to obtain the desired pH value (pKa (MESH)= 6.2, experimental pH range (5.50–7.50). pH values are measured with a microprocessor pH meter HANNA 210 equipped with a combined electrode glass and calibrated with commercial buffers (pH 4.00 and 7.00). Then aliquots ($v = 0.100 - 0.200\ mL$) of an aqueous solution of the H_3L and H_2L ($C_L = 1\ g/L$ and $C_L = 10\ g/L$ respectively) was added, using a Gilson micropipet of 0.2 ml. After each addition, the resulting solution was left at least 2 min in order to reach equilibrium (and thus a constant absorption value). Addition was repeated until a maximum volume of 6 ml of the ligand's solution was added. The change in the total volume was neglected. For fixed pH environments, the apparent formation constants $logK'_{xyz}$ was calculated from the equilibrium of the reaction of formation of these complexes. The absorption values for the undissociated (A_F) and the totally dissociated (A_I), sacrificial complex ($Gd-H_4Ch$), are used as determined in experiments using pure Chrome Azurol S, and an excess of Gadolinium(III) (performed at pH intervals of 0.25). Assuming various integers for the Gadolinium and organic acid's stoichiometry, a formation constant is calculated for each added amount of ligands and corresponding absorption value. The results are rejected when a systematic variation of $logK'_{xyz}$ occurs with increasing added-up amount of ligands or when individual values of $logK'_{xyz}$ differed from the mean value by more than 2%.

3. Results and discussion

3.1. Indirect photometric detection study: expression of the stability constant of complexes Gd–ligands

The complexation reaction of gadolinium ions with acids studied in this work, given by general reaction (I):

$$xGd^{3+} + yL^{n-} + zH^{+} \rightleftharpoons (x,y,z) + nH_2O \quad (I)$$

- L^{n-} is ligand (acid) (n=3 for H_3L and n=2 for H_2L).
- We noted (x, y, z) to simplify the writing of complex formed.
- x, y and z are, respectively, the stoichiometric coefficients relating to the Gd^{3+} ion, acid studied in its basic form and the number of protons H^+ involved in complexation reaction.

The formation constant K_{xyz} (or stability constant β_{xyz}) of the complexes formed defined by equation (1):

$$K_{xyz} = [(x,y,z)] / \left([Gd^{3+}].[L^{n-}].[H^{+}]^z\right) \quad (1)$$

Additionally, a conditional constant K'_{xyz} is defined in case of constant pH value (buffered solution):

$$K'_{xyz} = [(x,y,z)] / \left([Gd^{3+}].(C_L)^y\right) \quad (2)$$

3.1.1. Expression of stability constant $logK_{xyz}$ of complex Gd–H_2L

Where C_L represents the analytical concentration of the uncomplexed ligand, therefore, we have for H_2L $C_L = [L^{2-}]$ in our pH range because pH > pK_{a2} of this acid. Using this equality and Eq. (1) can be written as:

$$K'_{xyz} = [(x,y,z)] / \left([Gd^{3+}].[L^{2-}]^z\right) \quad (3)$$

$$K'_{xyz} = K_{xyz}.[H^{+}]^z \quad (4)$$

The formation constant K_{xyz} and the apparent constant of this complex defined by equation (5): $\log K_{xyz} = \log K'_{xyz} + z.pH$ (5)

3.1.2. Expression of stability constant $logK_{xyz}$ of complex Gd–H_3L

The chemical equilibrium and acidity constant of citric acid (H_3L) are:

$H_3L \longleftrightarrow H_2L + H^+ \; K_{a1} = 7.41\times10^{-4}$, K_{a1}

$H_2L^- \longleftrightarrow HL^{2-} + H^+ \; K_{a2} = 1.74\times10^{-5}$, K_{a2}

$HL^{2-} \longleftrightarrow L_3^- + H^+ \; K_{a3} = 3.16\times10^{-7}$, K_{a3}

$K_{a1} = \frac{[H_2L^-][H^+]}{[H_3L]}$, $K_{a2} = \frac{[H_2L^{2-}][H^+]}{[H_2L^-]}$ And $K_{a3} = \frac{[L^{3-}][H^+]}{[HL^{2-}]}$

The expression of the analytical concentration C_L of citric acid in the solution is given by the formula

$C_L=[L^{3-}]+[HL^{2-}]+[H_2L^-]+[H_3L]_{free} = [L^{3-}]\times(1 + [H^+]/K_{a3}+[H^+]^2/K_{a3}\times K_{a2}+[H^+]^3/K_{a3}\times K_{a2}\times K_{a1})$

For pH values between K_{a2} and K_{a3}, the ions

$[HL^{2-}]$ (OOC-CH_2-(HOOC)–C–(OH)–COO^-)

Predominate in the solution.

So $C_L = [HL^{2-}] = [L^{3-}] \times [H^+] / K_{a3}$

Therefore, the stability constant expressed by equation (1) takes the following expression:

$K_{xyz} = \{[(3, 2, z)] / [Gd^{3+}]^3 (C_L)^2\} (K_{a3})^2 \times [H^+]^{z-2}$

And the equation (2) become : $K_{xyz} = K'_{xyz} \times [H^+]^{-(z-2)} \times K_{a3}^{-2}$

So $logK'_{xyz} = logK_{xyz} - 2\,pK_{a3} - (z-2)\,pH$ (6)

In the first stage of the characterization of the gadolinium complexes with studied acids, we determined the compositions x, y, z and stabilities constants of these colorless complexes. The complexation of the ligands (acids) can be studied using a spectrophotometric method. Since the reagents (acids) and their gadolinium complexes don't possess a characteristic UV–visible absorption spectrum, a second ligand (called the sacrificial ligand) is introduced, this ligand must absorb in the UV–visible spectrum and form a colored complex with gadolinium (III). The dissociation of this colored complex has to cause large variations in the UV–visible spectrum which allows for the calculation of the concentration of the sacrificial complex ; using the formation constant of this colored complex, the concentration of the unknown complex can be obtained. Therefore, the sacrificial ligand must form a single colored complex of lower stability than the gadolinium complex under study. In this work, Sulfo–3"–dichloro–2",6"dimethyl–3,3'-hydoxy–4'–fuchsone–5,5'–dicarboxylic acid, often called Chrome Azurol S and notable H_4Ch, has been used as sacrificial ligand. Chrome Azurol S is a tetraprotic acid with pKa values of 2.25 ($H_3Ch^-/(H_2Ch^-)$, 4.71 (H_2Ch^{2-}/HCh^{3-}) and 11.82 (HCh^{3-}/Ch_4^-) (Langmyhr & Klausen 1963 p. 149). In the experimental pH range (5.50–7.50), the formation of H_4Ch , H_3Ch^- and H_2Ch^{2-} has been neglected. It is an indicator which is generally used for the photometric proportioning of the metal ions in solution (Dona & Verchere 1991 p. 533). In this work the interaction of the H_4Ch with gadolinium ions (Gd^{3+}), gives a colored reagent ($\lambda_{max} = 545\,nm$) of average stability for values of pH ranging between 5.50 and 7.50. The buffer ''MESH''. [2–(N–Morpholino) sulfonic ethane acid] was adopted to fix pH in the study of the sacrificial complex (Gadolinium–H_4Ch) and gadolinium–Ligands (complexes studied in this work). We chose this buffer because it does not present any interaction with Gd^{3+} ions and so we would be able to work in the range of pH where the stability of the sacrificial complex is maximal.

3.2. Formation of the colored sacrificial complex $Gd_x(HCh)_y$

The majority of organometallic complexes studied are colorless. Thus the study of the formation of the sacrificial complex $Gd_x(HCh)_y$ is very important, because this steps decisive parameters (composition and stability) of gadolinic complexes charactirazed in this work. In this sense, we have demonstrated, experimentally, that the composition and stability of the colored sacrificial complex (Gd–CAS) were determined, we found a complex type (3, 2, 3) and stability constant $logK_{323} = 16.27$ in pH range 5.50–7.50 (Ramshing et al. 1980 p. 165, Verchere &, Dona 1992 p. 437, Morin et al. 1994 p. 178, Hlaïbi et al. 2009 p. 310), the equilibrium reaction for this complex is

$$3Gd^{3+} + 2HCh^{3-} + 3H^+ \longleftrightarrows (3,2,3) + nH_2O \quad \text{(III)}$$

We use these results of sacrificial complex formed in solution, to study two colouress complexes Gd–Citrate ions and Gd–camphorate ions.

3.3. Composition and stability of the Gd (III) – Acids

The ligands (acids) are added separated to a colored solution containing sacrificial complex Gd_3HCh_2 , this complex will dissociate under effect of these ligands. To calculate the complex concentration of the HCh^{3-} ions, the absorption values of the totally complexed (A_F), and the completely dissociated (A_I) HCh^{3-} ions have to be determined. Then the following equations can be used :

$$[(x,y,z)] = \alpha \times C_L = C_L.(A - A_I)/(A_F - A_I) \quad (7)$$

α coefficient of sacrificial complex formation.

$$[HCh^{3-}]_{free} = C_L \times (A_F - A)/(A_F - A_I) \quad (8)$$

When the conditional constant K'$_{323}$ of the sacrificial complex is known, the concentration of free gadolinium ion ($[Gd^{3+}]$), can be calculated using Equations (7) and (8). Knowing the two concentrations of complex [(3, 2, 3)] and of $[Gd^{3+}]$, the concentration of the gadolinium complex under study [(x, y, z)] (balanced reaction I) can be determined using the gadolinium balance equation :

$$x.[(x,y,z)] = C_{Gd} - [Gd^{3+}]_{free} - 3[(3,2,3)] \quad (9)$$

C_{Gd} the initial gadolinium concentration and [(x, y, z)] the concentration of coloress complex formed.
In a similar way, the concentration of the free ligand is obtained by Eq. (10) :

$$(C_{L^{n-}})_{free} = (C_{L^{n-}})_{initial} - y[(x\ y,z)] \quad (10)$$

It should be also noted that a perfect knowledge of the characteristics of the sacrificial colored complex (Gd_3HCh_2) is necessary. The determination of the composition and the stability of the sacrificial complex and the precision of the conditions of its formation are paramount stages to apply the indirect photometry detection. In each experiment, the ligands completely deprotonate are added stepwise in order to measure the absorption at different values of the overall initial concentration of these studied ligands. The correct K'_{xyz} looked for by varying X and Y in order to obtain a constant value of K'_{xyz} for all values of $C_{L^{n-}}$ added in solution. If $\log K'_{xyz}$ is determined at different pH, the slope of the $\log K'_{xyz} = f(pH)$ plot reveals the number z of protons that is very necessary for the formation of the studied gadolinium complexes by the use of Eq. (5), since the value of K_{xyz} is independent of pH.

3.4. Determination of the composition and the stability constant of complexes Gd–Acids

With an aim of determining the composition and the stability constant of the gadolinium–citrate ions and gadolinium–Camphorate ions, we monitoring the evolution of the absorbance during the disappearance of the sacrificial complex by the addition of increasing quantities of ligands. For a given volume ($50mL$) of a solution containing sacrificial complex (3,2,3) ($10^{-4}M$), we added increasing quantities of L^{3-} and L^{2-} ions with known concentration. The spectrophotometric study carried out with fixed wavelength ($\lambda_{max} = 545nm$), showed a reduction in the absorbance of the solution progressively with the addition of the acids (figure 1). The dissociation of the sacrificial complex, relating to the reduction in the absorbance by the addition of ligands, is done in favor of the formation of the colorless complex between Gd^{3+} and studied acids. The curves C1 and C2, in figure 1, of complexes formed in solution Gd– H_3L and Gd– H_2L respectively, clearly show that the absorbance decreases and stabilizes. This stability indicates that all Gd^{3+} ions, initially present in the solution have reacted with ligands.

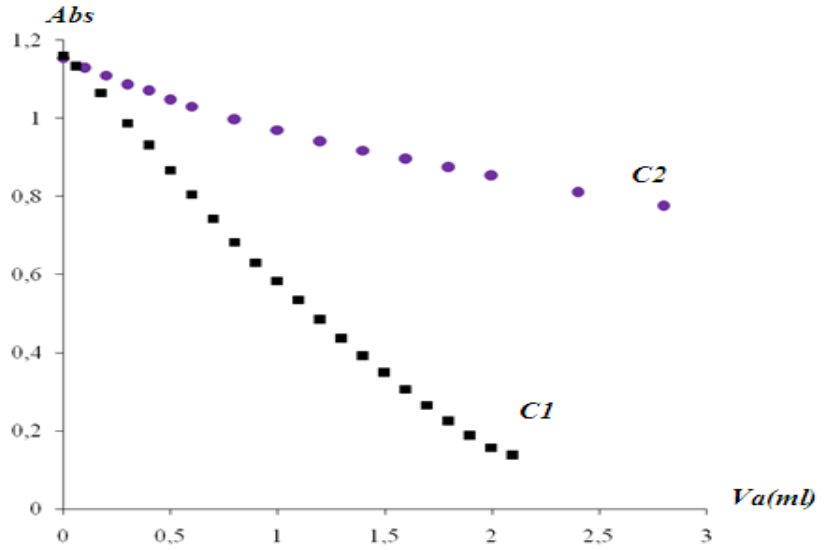


Fig. 1: Decomposition of Colored Sacrificial Complex by Addition of H_3L and H_2L Ions.
C1: Gd–H_3L, Mass concentration $1g/L$, pH=6, 46 and *C2* : Gd–H_2L, Mass concentration $10g/L$, pH = 6,27

Knowing the concentration of gadolinium ions and the quantity of ligands (added volume Va of acid), necessary to reach this stage of absorption, we could determine the molar ratio $q = ([Gd^{3+}]/[acid])$, involved in the complexation reaction. The preceding experiment was carried out for different values of pH between 5.50 and 7.50, the way in which the absorption decreases, depends on the pH of the medium and on the formation constant of the detected complexes, as well as on the absorption values (A_I) and (A_F) of the free and totally complexed Chrome Azurol S. Analyzing the experimental data with the computer program written from the balanced reaction (I), the results confirm the reproducibility of the molar ratio $q = ([Gd^{3+}]/[acid]) = x/y$ and to determine the composition and the stability constant K'_{xyz} . This program is not a theoretical modeling (but this is a translation of the reaction steps of the balance (I) for ease of calculation). In figure 2 we represent an example of calculating the ratio q at pH 6.46 of complex Gd- H_3L, where we inserted the two experimental values: V_a and Abs corresponds for each added volume V_a of ligand, to seek the values of X and Y to the value of $\log K'_{xyz}$ which remains constant.

Systeme Gd-Acide

CL =	1,00E-04	pH =	6,46
CGd =	1,50E-04	Ai =	0,225
MM =	294,1	Af =	1,535
Log(Kc) =	6,57	Acid =	Citric
Kc =	3715352,291		
X =	4,00	Cm =	1
Y =	2,00	V total =	50
Complex		Gd 4,0	Citric 2,0

Va	A	Gd-CAS	L	Gd	Gd-Acide	Acide	T	T'	K'	CAcide	B	LogK'xyz
0,55	0,838	4,679E-05	5,321E-05	3,8E-05	1,63E-05	4,835374E-06	2,101065E-18	2,338084E-11	3,314717E+23	3,740224E-05	0,468	23,52
0,60	0,805	4,427E-05	5,573E-05	3,6E-05	1,75E-05	5,728795E-06	1,602214E-18	3,281909E-11	3,335062E+23	4,080245E-05	0,443	23,52
0,65	0,775	4,198E-05	5,802E-05	3,3E-05	1,86E-05	6,909744E-06	1,248869E-18	4,774456E-11	3,127198E+23	4,420265E-05	0,420	23,50
0,70	0,743	3,954E-05	6,046E-05	3,1E-05	1,98E-05	7,997706E-06	9,533953E-19	6,396330E-11	3,247266E+23	4,760286E-05	0,395	23,51
0,75	0,711	3,710E-05	6,290E-05	2,9E-05	2,09E-05	9,135547E-06	7,235887E-19	8,345821E-11	3,466461E+23	5,100306E-05	0,371	23,54
0,80	0,683	3,496E-05	6,504E-05	2,7E-05	2,19E-05	1,059218E-05	5,649581E-19	1,121943E-10	3,455947E+23	5,440326E-05	0,350	23,54
0,85	0,655	3,282E-05	6,718E-05	2,6E-05	2,29E-05	1,207842E-05	4,379798E-19	1,458883E-10	3,578076E+23	5,780347E-05	0,328	23,55
0,90	0,630	3,092E-05	6,908E-05	2,4E-05	2,37E-05	1,379189E-05	3,464109E-19	1,902161E-10	3,597638E+23	6,120367E-05	0,309	23,56
0,95	0,609	2,931E-05	7,069E-05	2,3E-05	2,44E-05	1,578957E-05	2,826947E-19	2,493105E-10	3,463051E+23	6,460388E-05	0,293	23,54
1,00	0,584	2,740E-05	7,260E-05	2,2E-05	2,52E-05	1,753520E-05	2,200120E-19	3,074833E-10	3,730145E+23	6,800408E-05	0,274	23,57
1,05	0,566	2,603E-05	7,397E-05	2,1E-05	2,58E-05	1,975309E-05	1,824386E-19	3,901847E-10	3,627966E+23	7,140428E-05	0,260	23,56
1,10	0,555	2,519E-05	7,481E-05	2E-05	2,62E-05	2,243407E-05	1,621974E-19	5,032874E-10	3,207717E+23	7,480449E-05	0,252	23,51
1,15	0,537	2,382E-05	7,618E-05	1,9E-05	2,68E-05	2,466216E-05	1,330345E-19	6,082221E-10	3,308587E+23	7,820469E-05	0,238	23,52
LogK'moyen =												23,54

Fig. 2: Example of Program Used to Calculate the Compositions X, Y and Stability $\log K'_{xyz}$.

C_m : Mass concentration ($1g/L$), V_a : volume of acid, A =Abs experimental absorbance, *Kc* : constant of colored sacrificial complex, $\log K'_{xyz} moy = 23,54$ for $q = x/y = 4/2$ and $pH = 6.46$

The calculations are repeated for different experimental values of pH between 5.50 and 7.50. We obtained a molar ratio $q = x / y$ for Gd- H_3L equal 4:2 and 2:2 for H_2L. The data-processing treatment of the preceding experimental results, shows that these di and tetra-nuclear complexes are formed between the gadolinium ions and ligands, resulting from the interaction of two Gd (III) ions equivalents with two equivalents of H_2L and four Gd (III) ions for H_3L, so a molar ratio q and conditional constant $\log K'_{xyz}$ remains the same for each fixed value of pH between 5.50 and 7.50 for two complexes formed. The constants and the molar ratio q at differents values of pH are given in Table 2.

Table II: The Conditional Stability of the Two Complexes Detected

Gd–H_3L	pH	5.50	5.63	5.83	6.02	6.24	6.46
	$\log K'_{42z}$	26.00	25.70	24.99	24.48	24.08	24.53
Gd–H_2L	pH	------	5.62	5.85	6.07	6.27	6.50
	$\log K'_{22z}$	------	11.62	11.14	10.69	10.28	9.82

Buffer ($MES^- / MESH$), $\lambda_{max} = 545$ nm , $l = 1cm$, $\left[HCh^{3-}\right]_{total} = 10^{-4} M$

Therefore, for the complexation reaction, results of $logK'_{xyz}$, the reactions (I) and (II) and the eqution (1), (2), (5) and (6) allow us to write the following expressions for each complex:

3.4.1. Gd–H_3L

$$4Gd^{3+} + 2L^{3-} + zH^+ \rightleftharpoons (4,2,z) + nH_2O \quad \text{(IV)}$$

$$K'_{42z} = [(4,2,z)] / \left(\left[Gd^{3+}\right]^4 . (C_L)^2\right) \quad (11)$$

So, $\log K'_{42z} = \log K_{42z} - 2pK_{a3} - (z-2)pH$ (12)

3.4.2. Gd–H_2L

$$2Gd^{3+} + 2L^{2-} + zH^+ \rightleftharpoons (2,2,z) + nH_2O \quad \text{(V)}$$

$$K'_{22z} = [(2,2,z)] / \left(\left[Gd^{3+}\right]^2 . \left[L^{2-}\right]^2\right) = K_{22z} \times \left[H^+\right] \quad (13)$$

And $logK'_{22z} = logK_{22z} - z.pH$ (14)

For two complexes detected, the results in table 2 combined with equations (12) and (14) allow to plot functions $logK'_{xyz} = f(pH)$ for two complexes formed, hence determine the number z of protons H^+ involved in the reaction obtained from the straight lines. The evolution of $logK'_{xyz}$ at different pH values represented in figure 3.

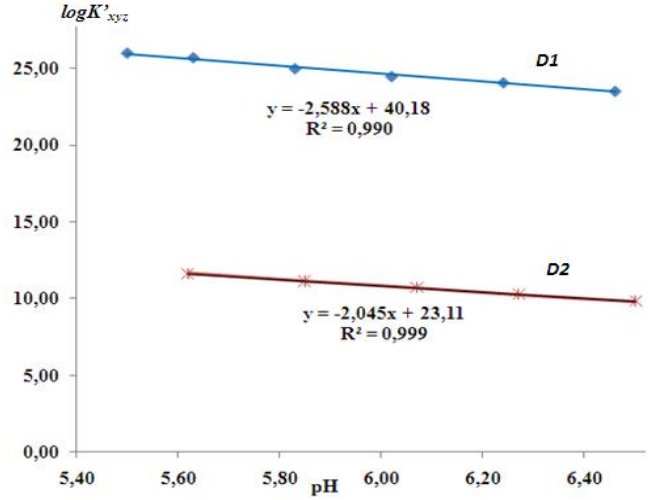


Fig. 3: The Evolution of $logK'_{xyz}$ at Different pH Values. D1: $logK'_{42z}$ =f (pH) of Complex Gd– H_3L and D2: $logK'_{22z}$ =f (pH) of Complex Gd– H_2L

This evolution of $logK'_{xyz}$ =f(pH) is linear and the slope p of the straight line is equal to ≈ –5/2 for complex Gd–H_3L and -2 for complex Gd–H_2L. So, the value of $-(z-2) = p \approx -5/2 \Leftrightarrow z = 9/2$ for Gd– H_3L and for Gd– H_2L $-z = p = -2 \Leftrightarrow z = 2$ represents the number of protons H^+ involved in the formation of two complexes respectively. The Equations (12) and (14) allowed us to calculate the stability constants $logK_{xyz}$ for theses two complexes, the experimental results obtained by the IPD are $logK_{42(9/2)} - 2pK_{a3} = 40.18 \pm 0.01$ with pK_{a3} = 6.50, so $\log K_{42(9/2)} = 53.18 \pm 0.01$ ($K_{42(9/2)} = 1,514.10^{53}$) and $logK_{222} = 23.11 \pm 0.01$ ($K_{222} = 1,288.10^{23}$) for Gd–H_3L and Gd–H_2L respectively.

Consequently, the spectrophotometric results concerning the interaction of the Gd(III) ion with H_2L show that the complexation reaction uses two Gd(III) ions, two carboxylates and fixation of two H^+ protons, but in the case of complex Gd– H_3L, there are four Gd(III) ions interact with two ligands and the intervention of 9/2 H^+. So, by comparing with other works on the complexes of the gadolinium ion (Hlaïbi et al. 2009 p. 310, Riri et al. 2014 p. 130, Riri et 2016 p. 1478), we have given the general formulas of these two complexes Gd-Citrate and Gd-Camphorate, therefore the both formulas are $Gd_4Citrate_2.4NO_3.nH_2O$ and $Gd_2Camphorate_2.2NO_3.mH_2O$.

Finally, we have obtained one dinuclear complex type (2,2,2) for camphoric acid in pH range 5.50 – 7.50, and one tetranuclear complex type (4,2,9/2) for the complex Gd–Citric acid in 5.50 <pH <6.50; but for pH values between 6.50 and 7.50 the study of the formation of complex Gd–Citric acid is not treated in this work.

4. Conclusion

In this work, we have identified and characterized two new polynuclear and plydentate complexes of gadolinium ion in aqueous solutions and in a pH region 5.50 to 7.50, using the indirect photometry detection. This technique was used successfully to determining the composition, and the stability of these major complexes formed in very dilute sulution, so we obtained two types of composition (2, 2, 2) for complex Gd–H_2L and (4,2,9/2) 2, 9/2 for complex Gd–H_3L. The stabilities of these new godolinium complexes are $logK_{42(9/2)} = 53.18 \pm 0.01$ and $logK_{222} = 23.11 \pm 0.01$ for Gd–H_3L and Gd–H_2L respectively. We also mentioned that the acidity of the medium has a very important in determining the nature of the chelation site formed: bidentate and tetradentate (Hlaïbi et al. 2009 p. 310, Riri et 2016 p. 1478).

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