



Vibrational spectra of two Fe(III)/EDTA complexes useful for iron supplementation

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ARTICLE INFO

Article history:

Received 13 October 2009

Received in revised form

18 November 2009

Accepted 30 November 2009

Keywords:

Iron supplementation

Fe(III)

EDTA complexes

Infrared spectra

Raman spectra

ABSTRACT

The infrared and Raman spectra of $\text{Na}[\text{FeEDTA}(\text{H}_2\text{O})]\cdot 2\text{H}_2\text{O}$ and $\text{Na}_4[(\text{FeEDTA})_2\text{O}]\cdot 3\text{H}_2\text{O}$ (EDTA = tetra anion of ethylenediaminetetraacetic acid), two complexes proposed as adequate for iron supplementation, were recorded and analyzed in relation to its structural peculiarities. Some comparisons between the recorded spectra are also presented, and the characteristics of the carboxylate motions as well as those of the metal-to-ligand vibrations are discussed in detail.

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1. Introduction

Anemia and iron deficiency are the most frequent nutritional problems on a worldwide scale, affecting approximately 2 billion people, 85% of whom suffer it as a consequence of deficient iron ingestion or low absorption of an adequate iron amount [1,2]. It can be estimated that, at present, 34% of the world population suffers from iron deficiency, 80% of whom live in developing countries [2]. The principal risk groups include children, adolescents, pregnant women, and women in reproductive age [2,3]. Studies carried out by WHO demonstrated that in developing countries, 47% of the women in reproductive age are, at least, slightly anemic [3,4].

The adverse effects of iron deficiency include lower growth rate and impaired cognitive scores in children and poor pregnancy outcome and lower working capacity in adults. The main cause of this phenomenon in less industrialized countries as in developing countries is the poor bioavailability of iron in the diets, caused by the type of ingested foods, the alimentary habits and the socio-economic situations [2]. Recommended daily intakes of dietary iron for normal infants are 1 mg/kg/day and for children and for adolescent male and female, 10, 12, and 15 mg/day, respectively. Women

in reproductive ages require about 15 mg/day, whereas adult men and postmenopausal women require only 10 mg/day [5].

Strategies for combating iron deficiency include iron supplementation, food diversification and food fortification [3]. Food fortification is being recognized as a sustainable, relatively simple, and realistic way to reduce and prevent iron deficiency. The main advantage of these fortification programs, compared with the medical supplementation, is that they do not require the consumer's indulgence and that they are relatively cheap. However, fortification of foods, such as cereal flours, is difficult as the added iron either causes organoleptic changes during storage and preparation or has a low bioavailability. In general, water-soluble iron compounds (such as ferrous sulfate) have an acceptable bioavailability but cause unacceptable organoleptic changes during storages and/or preparation of the flours. In contrast, water-insoluble iron compounds generally do not cause organoleptic changes during storage or food preparation of cereal flours, but it may be poorly absorbed. Besides, it is also necessary to keep in mind the presence of activators and inhibitors and their possible effects in iron absorption [6].

Therefore, an ideal supplement would be a substance with high bioavailability without organoleptic effects and which absorption is not strongly influenced by the action of inhibitors. Fe–Na–EDTA complexes have these characteristics, and were recommended as the most suitable iron-fortifying agents for developing countries [7,8], although their use is restricted at the moment to experimen-

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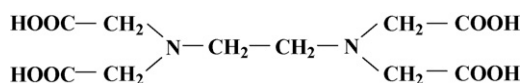


Fig. 1. Schematic structure of ethylenediaminetetraacetic acid (H_4EDTA).

tal rehearsals because they have not still completely characterized completely [2,3,9,10].

As part of a research project devoted to the characterization of iron complexes with recognized pharmacological activity, we have prepared and investigated two iron(III) complexes of EDTA, namely $\text{Na}[\text{FeEDTA}(\text{H}_2\text{O})]\cdot 2\text{H}_2\text{O}$ and $\text{Na}_4[(\text{FeEDTA})_2\text{O}]\cdot 3\text{H}_2\text{O}$ and in this paper we present a complete vibrational-spectroscopic study of them.

H_4EDTA (ethylenediaminetetraacetic acid) is one of the best known and most widely used chelating agents in both analytical chemistry [11] and medicine [12–14]. It is a potentially hexadentate chelating ligand (see Fig. 1), as each of the nitrogen atoms has a free electron pair and the molecule possesses four acidic hydrogens ($\text{p}K_1 = 2.0$, $\text{p}K_2 = 2.67$, $\text{p}K_3 = 6.16$, $\text{p}K_4 = 10.26$) [13]. The $(\text{EDTA})^{4-}$ anion is capable of complexing almost every metal cation in the Periodic Table and the six coordinating groups are able to occupy four, five or six coordination sites around a central metal cation. The degree of EDTA–metal complex formation normally depends on the stability of the particular metal–complex and the pH-value of the environment.

2. Experimental

All the employed reagents and solvents were analytical grade. Pure $\text{Fe}(\text{OH})_3$ was obtained, according to the procedure described by Brauer [15]. The investigated complexes were prepared using known synthetic procedures, as follows:

$\text{Na}[\text{FeEDTA}(\text{H}_2\text{O})]\cdot 2\text{H}_2\text{O}$. This complex was prepared by treating 0.01 mol (1.07 g) of $\text{Fe}(\text{OH})_3$ with 0.01 mol (2.92 g) of ethylenediaminetetraacetic acid and 0.01 mol (0.40 g) of NaOH , in 40 mL of distilled water at 80–90 °C for 20 min. Slow evaporation at room temperature of the resulting yellow solution produced well-formed brown crystals [16].

$\text{Na}_4[(\text{FeEDTA})_2\text{O}]\cdot 3\text{H}_2\text{O}$. A slurry of 0.01 mol of $\text{Fe}(\text{OH})_3$ in 50 mL distilled water was allowed to react with the same molar amount of the disodium salt of ethylenediaminetetraacetic acid (3.72 g) for several minutes at 80–90 °C. The resulting dark red solution had a pH of about 9.0. A crystalline red solid was readily obtained after slow addition of DMF [17].

Both complexes were characterized by elemental chemical analysis and X-ray powder diffractometry, using a Philips PW 3710 diffractometer and monochromatic $\text{Cu-K}\alpha$ radiation. The obtained powder diagrams were compared with the theoretical diagrams generated by the program POWDERCELL [18] on the basis of the known single crystal data [19,20].

The infrared spectra in the spectral range between 4000 and 250 cm^{-1} were recorded on KBr pellets with a Nicolet Magna 550 FTIR instrument. A total of 32 scans were accumulated. Raman spectra, in the same range were obtained with the FRA 106 Raman accessory of a Bruker IFS 66 FTIR instrument. A total of 60 scans were accumulated, using the 1064 nm line of a solid state Nd:YAG laser for excitation. Spectral resolution was $\pm 4\text{ cm}^{-1}$ for both spectral measurements.

3. Results and discussion

3.1. Structural characteristics of the complexes

Structural information is available for both investigated compounds. Schematic drawings showing the coordination characteristics of Fe(III) in the complexes are depicted in Fig. 2. The most relevant structural aspects are summarized as follows:

$\text{Na}[\text{FeEDTA}(\text{H}_2\text{O})]\cdot 2\text{H}_2\text{O}$. This complex belongs to the monoclinic Cc space group with $Z = 4$. It presents a pseudo-pentagonal bipyramidal structure with a seven coordinated Fe(III) cation, bonded to the four ionized carboxyl oxygen atoms and the two nitrogen atoms from the hexadentate EDTA ligand whereas the seventh donor is the O-atom from a water molecule [19].

$\text{Na}_4[(\text{FeEDTA})_2\text{O}]\cdot 3\text{H}_2\text{O}$. The dimeric complex crystallizes in the monoclinic space group $P2_1/n$ with $Z = 4$. The coordination polyhedron around each Fe(III) in the dinuclear $[(\text{EDTA})\text{Fe}-\text{O}-\text{Fe}(\text{EDTA})]^{4-}$ anion approximates to a distorted octahedron with the bridging oxygen atom approximately *trans* to one of the nitrogen atoms of

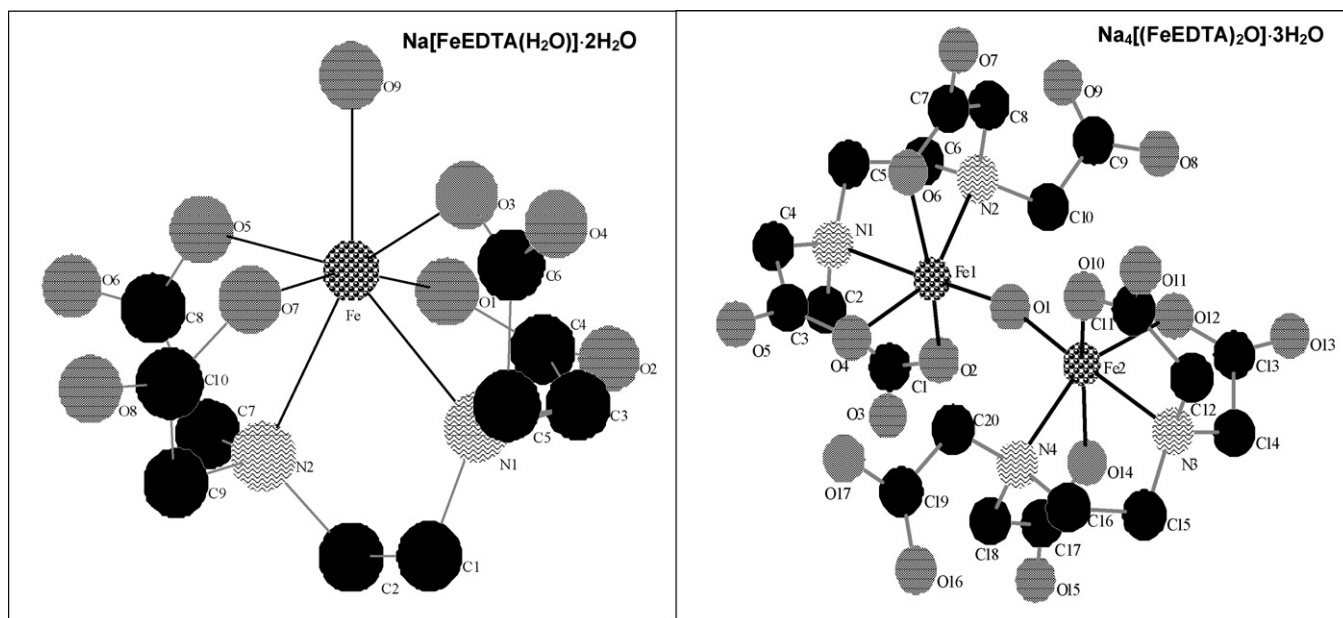


Fig. 2. Schematic drawing of the structures of the investigated complexes, adapted from the corresponding crystallographic studies [19,20].

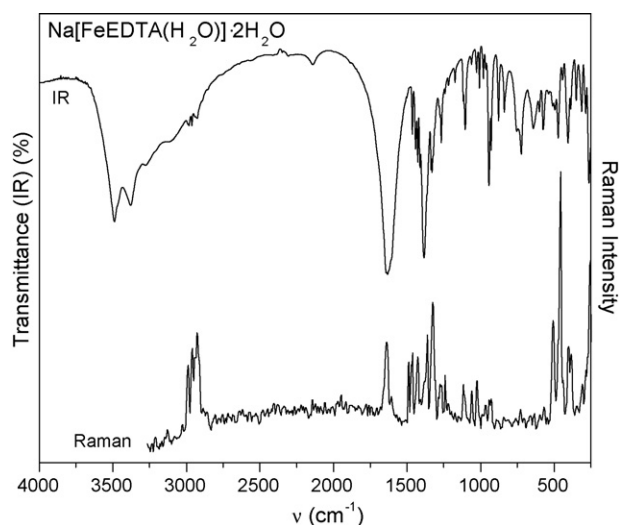


Fig. 3. FTIR and FT-Raman spectra of the Na[FeEDTA(H₂O)]·2H₂O complex.

the EDTA group. Thus, three of the tetraacetate groups have one of their oxygen atoms involved in coordination while the fourth is turned away from the central iron cation. The three oxygen atoms and the second nitrogen atom conform a plane, with the iron atom slightly displaced outside it. The Fe–O–Fe bond angle is 163.2° [20].

3.2. Infrared and Raman spectra

The spectra of both investigated compounds are very complex presenting a great number of bands in all spectral ranges. Consequently, it seems very difficult to attempt a detailed assignment of them. Notwithstanding, the most important and characteristic vibrational modes could be identified and comparisons between the investigated compounds could be made, allowing some general conclusions on their vibrational behavior. The spectra of the two investigated complexes are shown in Figs. 3 and 4, and as it can be seen, they present very similar spectral patterns, pointing clearly to relatively similar coordination characteristics. The proposed spectral assignments are presented in Table 1 and have been performed on the basis of previous studies [21–24] and with the aid of some standard references [25,26].

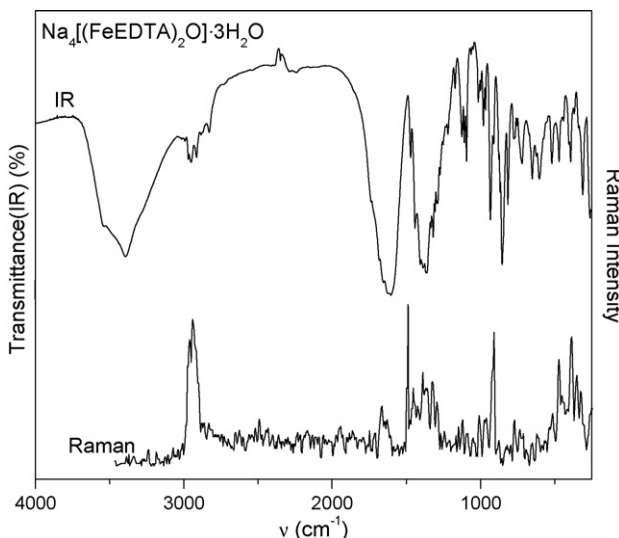


Fig. 4. FTIR and FT-Raman spectra of the Na₄[(FeEDTA)₂O]·3H₂O complex.

Table 1

Assignment of the most characteristic IR and Raman bands (in cm⁻¹) of the two investigated complexes.

Na[FeEDTA(H ₂ O)]·2H ₂ O		Na ₄ [(FeEDTA) ₂ O]·3H ₂ O		Assignment
IR	Raman	IR	Raman	
3493 s		3392 vs, br		$\nu_{as}(\text{OH}) \text{H}_2\text{O}$
3378 s				$\nu_s(\text{OH}) \text{H}_2\text{O}$
3275 w				
3207 sh				
3104 sh				
2985 w	2989 m	2991 vw	2970 m	
2966 w	2960 m	2969 w	2960 m	
2925 w	2928 m	2955 w	2940 m	$\nu(\text{CH}_2)$
		2912 w	2920 m	
1638 vs	1640 m	1654 vs	1667 m	$\nu_{as}(\text{COO}^-)$
		1630 vs	1627 w	$\nu_{as}(\text{COO}^-)$ free
1602 sh	1609 m	1603 sh	1607 vw	Bending HOH
1503 sh	1490 m		1492 s	
1464 m	1461 m	1471 m	1473 vw	
1441 m	1442 sh	1440 s	1458 m	$\delta(\text{CH}_2)$
1427 m	1426 m		1423 vw	
1412 m	1410 w			
		1405 s		$\nu_s(\text{COO}^-)$ free
1384 vs	1382 w	1387 s	1388 m	$\nu_s(\text{COO}^-)$
1362 sh	1361 m	1361 s	1368 m	$\delta(\text{CH}_2)$
1336 m		1333 m		$\delta(\text{CH}_2) + \nu(\text{C-CO}_2)$
1329 m	1325 m	1318 m	1323 m	
1309 sh	1307 w	1307 w		
1284 vw	1287 w	1290 w	1293 w	
1277 vw	1277 w			
1267 m	1267 w	1272 m		$\delta(\text{CH}_2)$
1242 w	1242 m	1252 w		
1218 w	1217 w	1218 w		
1175 w		1172 m		$\nu(\text{CNC})$
		1126 m	1148 w	
1118 w	1117 m	1108 m	1118 w	
1104 m	1107 w	1094 m	1093 w	$\nu(\text{CN})$
1062 w	1062 w	1063 w	1053 w	$\nu_{as}(\text{C}_3\text{N})$
1028w	1027 w	1014 m	1008 w	
1008 m	1008 vw	997 w		
982 w	988 vw	980 m		
964 vw	968 w	965 m	959 w	
943 s	943 w	933 s	918 sh	
928 m	928 vw	910 w	912 s	$\nu(\text{CC})$
879 m		879 w		
		853 s	874 w	$\nu_{as} \text{Fe-O-Fe}$
839 m		814 m		$\nu_s(\text{C}_3\text{N})$
754 w		754 m	769 w	$\delta(\text{C=O})$
724 s		719 m	709 w	$\rho(\text{CH}_2)$
674 w		671 w		$\rho_w(\text{COO}^-)$
641 m		651 m	649 w	$\rho(\text{H}_2\text{O})$
600 w		602 m	619 w	$\pi(\text{C=O})$
576 m		575 sh		$\rho_w(\text{H}_2\text{O})$
538 w		554 w	534 w	
511 w	510 m	518 m	514 w	
495 w				
473 m	465 vs	470 m	475 m	$\nu(\text{Fe-N}) + \rho_w(\text{H}_2\text{O})$
442 w	438 w	440 w	449 w	
405 m	406 m			$\nu(\text{Fe-O(H}_2\text{O)})$
		392 m	389 m	$\nu_s \text{Fe-O-Fe}$
		367w		
388 w	383 w	337w	354 m	
350 m	344 vw	310 s	324 w	$\nu(\text{Fe-O})$
312 m	309 w			
286 m	283 w			
263 s	262 s	261 s	260 w	

vs, very strong; s, strong; m, medium; w, weak; sh, shoulder.

In the higher frequency region a very broad and strong IR band, originated in the O–H stretchings of the H₂O molecules, is observed for both complexes. For the monomer, the $\nu_{as}(\text{OH})$ and $\nu_s(\text{OH})$ components can be differentiated in the infrared spectrum (3493 and 3378 cm⁻¹, respectively). On the other hand, for the dimer, there is only one broad and strong band centered at 3392 cm⁻¹. On the lower frequency side of these bands some weak or medium intensity bands, related to the stretching vibrations of the CH₂ groups

were observed. The $\delta(\text{HOH})$ bending mode can be identified as a component of the central and most intense IR band at around 1600 cm^{-1} as well as to the corresponding Raman band in the same spectral region.

As mentioned above, two different types of carboxylate groups are present in the dimeric complex, as three of them participated in bonding to the metal centers whereas the other one remains not bonded. In this way, one expects two groups of carboxylate stretching vibrations which appear as components of a strong IR and Raman band. In Table 1 the non-bonded group has been identified as $\nu_{\text{as}}(\text{COO}^-)_{\text{free}}$. The corresponding $\nu_{\text{s}}(\text{COO}^-)$ vibrations have the same characteristics. On the contrary, in the monomer, only one type of carboxylate group is present, as the four are bonded to the Fe(III) center. Therefore, only one signal is assigned to the $\nu_{\text{as}}(\text{COO}^-)$ and $\nu_{\text{s}}(\text{COO}^-)$ vibrations in this case.

The mentioned carboxylate stretching vibrations satisfactorily fulfill some well-known criteria regarding its spectral position and the energy differences between the antisymmetric and symmetric vibration [26,27]. This energy difference ($\Delta\nu$) for the monodentate coordinating groups is 254 cm^{-1} in the monomeric complex and 267 cm^{-1} in the dimeric complex. As expected, these $\Delta\nu$ values are somewhat higher than that of the ionic (or free) carboxylate group (225 cm^{-1} in the dimer).

In assigning deformational modes of the CH_2 groups we have not differentiated between different kinds of possible motions. Only the characteristic rocking (ρ) mode was separately identified. Some of these modes, as well as other skeletal modes are probably coupled together and cannot be considered as “pure” vibrations.

The positions of the ligand-to-metal vibrations were obtained by the comparison of the complex spectra with those of the corresponding free ligand and with results of previously investigated complexes [21,23,26]. These bands are found in similar ranges as the ones for these other complexes. In the case of the monomer three bands related to $\nu(\text{Fe-Ligand})$ vibrations are found in agreement with the three types of bonds present in this complex: Fe–N, Fe–O(EDTA) and Fe–O(H_2O). On the other hand, we have identified two bands corresponding to the $\nu(\text{Fe-O})$ and $\nu(\text{Fe-N})$ stretchings, for the dimeric complex. Besides, in this case two additional IR bands, absent in the monomer, were found at 853 cm^{-1} (874 in the Raman) and 392 cm^{-1} (389 in the Raman). They can be assigned to the Fe–O–Fe antisymmetric and symmetric stretching modes, respectively, involving the oxygen bridging moiety. According to the literature, if the oxo M–O–M bridge is angular both stretching vibrations will be IR and Raman active, with the antisymmetric mode stronger in the IR spectrum and the symmetric one stronger in the Raman spectrum [26].

To conclude, this spectroscopic investigation extends the knowledge on the general physicochemical properties of two interesting supplementation systems for iron and brings a new and easy tool for their rapid and effective characterization.

Acknowledgements

This work has been supported by the Universidad Nacional del Centro de la Provincia de Buenos Aires, the Universidad Nacional de La Plata and the Consejo Nacional de Investigaciones Científicas y Técnicas de la República Argentina, CONICET. The authors are members of the Research Career from this organism.

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