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Versatility of guanidoacetic acid coordination modes and synthesis of its new zinc complex

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ABSTRACT

Guanidinoacetic acid (GAA) is an amino acid involved in several biological processes including renal activity since it is synthesized mainly in the kidneys, insulin metabolism, creatine/phosphocreatine synthesis and recently as experimental nutrient for multiple sclerosis treatment. Given its biological role, some interactions between GAA and its complexation with essential and toxic metal ions have been previously investigated, both in aqueous medium with Ni(II), Co(II), Cu(II), Zn(II), Cd(II), and Pb(II), as well as in the synthesis of complexes in solid phase. This study presents the versatile coordination modes of GAA and reports its novel solid zinc complex. GAA complexation ranges from the usual α-nitrogen and oxygen bidentate coordination to a paddlewheel monodentate-oxygen mode in a Cu_2GAA_4 complex. The novel solid GAA zinc complex has only been succeeded to be synthesized in the presence of copper(II) salt, being characterized by single-crystal structure refinement using X-ray diffraction and mid and far-Fourier Transform Infrared spectroscopy. The results showed that the synthesized complex, $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ (**1**) , exhibits a tetrahedral geometry with an oxygen-carboxylate GAA monodentate coordination complemented by three chloride ligands and a water bridge linked to a monoprotonated GAA species. Hydrogen bonds play a crucial role in the stabilization of **1**, especially between $Zn(GAA)Cl^{3-}$ and its cation ion, $HGAA^+$. Infrared spectroscopy of **1** presented a band at 412 cm^{-1} and three bands at 291, 273 and 239 cm^{-1}, corresponding to Zn-O and Zn-Cl stretching modes, respectively. The different coordination modes of guanidinoacetate ion and its complexation with zinc and copper(II), as well as the way the hydrogen bonds stabilize their structures may help to further understand the diverse biochemical processes involved in this amino acid.

1. Introduction

Guanidinoacetic acid (GAA), or Glycocyamine ($C_3H_7N_3O_2$), is a naturally occurring amino acid that is a precursor of creatine and phosphocreatine [1,2], which is recently reported as a key player in high-phosphate bioenergetics and an experimental nutrient for multiple sclerosis treatment [3–5] . GAA is synthesized in mammalian organisms, predominantly in the acinus of kidney tubules, and is converted into creatine in the liver [1,2].

GAA belongs to the guanidino compounds that also include L-Arginine (Arg), creatine (CT), and phosphocreatine (PCT), all of them having Arg as a precursor [6]. The scheme in Fig. 1 depicts the biological metabolism of GAA from an Arginine precursor to creatine synthesis through its methylation and subsequent phosphorylation of the guanidino group, leading to the formation of phosphocreatine.

GAA participates in several biological processes such as kidney and renal metabolism, cholesterol production, thyroid metabolism, insulin production, epileptic seizures, and in guanidino methyl transferase role and its dysfunction [4,7–15]. In addition, GAA has been recently employed as supplemental for multiple sclerosis, improving creatine levels in the brain even better than creatine addition itself, and having a positive influence on demyelination, GABA (Gamma-aminobutyric acid) modulation, glutamate uptake, and the decrease of oxidative stress [5d,15–17].

Due to the biological roles of GAA, its complexation behavior has been investigated with essential and toxic metal ions in aqueous solution

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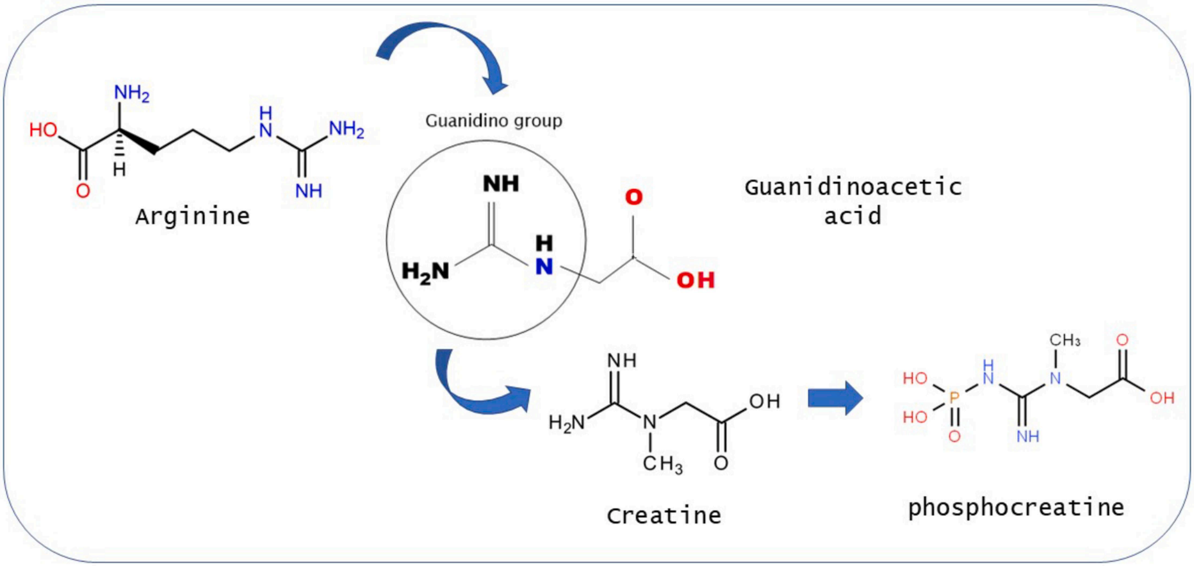

Fig. 1. Basic scheme of guanidinoacetic metabolism showing guanidino compounds (own authorship).

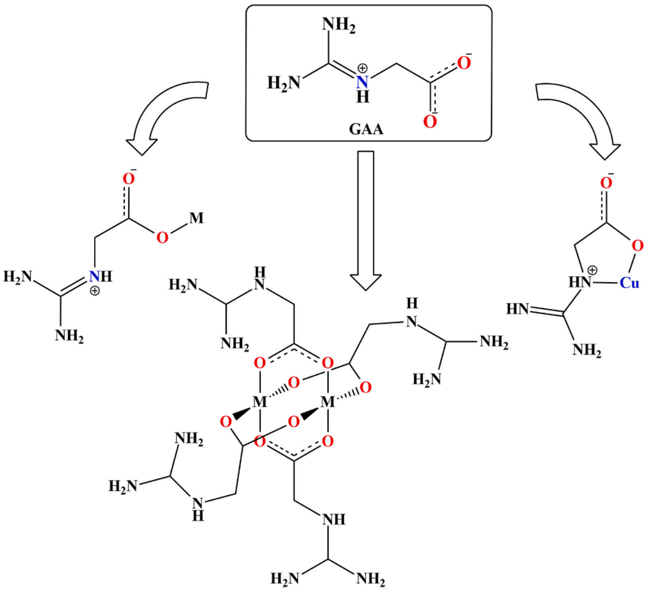

Fig. 2. Different modes of guanidinoacetate coordination: oxygen-monodentate, O,O'-bidentate and alpha-N,O'-bidentate chelating (own authorship).

and solid phase complexes [18,19]. The complexation of GAA in an aqueous medium was studied with the ions Ni(II), Co(II), Cu(II), Zn(II), Cd(II), and Pb(II) [20]. The guanidino-carboxylate interactions were also investigated in Cu(II), Co(II), Ni(II), and Zn(II) complexes of GAA with glutamic, aspartic, and glycine amino acids [18]. In addition, different complexes of Cu(II) with GAA have also been synthesized [2,18,20,21]. Experimental and theoretical studies on the complexes between cisplatin and GAA have also been conducted [19].

Considering the previously studied GAA complexes, different modes of coordination of its ion - guanidinoacetate - were observed. It is important to notice that as an amino acid, GAA may present its zwitter ion form with the alpha-amino group protonated and the carboxylate deprotonated. We will refer to the zwitter ion guanidinoacetate protonated in the alpha-amino group as GAA for the complexes for simplicity. In Fig. 2 different proposals for guanidinoacetate coordination are shown: O,O'-bidentate, alpha-N,O'-bidentate chelating, and the oxygen-monodentate. The usual amino acid α-nitrogen and oxygen coordination were observed in a group of monomeric complexes with Cu (II), Zn(II), and Ni(II) ions [18,20]. Due to the great basicity of the terminal imino-amino groups of the guanidino group, these terminal nitrogen atoms are not good coordination sites.

An interesting paddlewheel dimeric copper(II) GAA complex was also formed with η^2—*O*—*O*—carboxylate coordination in the Cu_2GAA_4 complex (Fig. 3). This complex exhibits an interesting anti-ferromagnetic coupling between the two copper ions, an intradimer interaction and an interdimer coupling, which was a temperature-driven interaction detected by electron paramagnetic resonance studies [20]. This anti-ferromagnetic coupling is accomplished through the oxygen atoms from the carboxylate-bridged ligand (Fig. 4).

Surprisingly, a desamidination reaction between two GAA species was observed in the presence of Cu(II) in the synthesis of a new complex $[Cu_2(oag)(GAA)(H_2O)]$ $NO_3{\cdot}2H_2O$, where oag, trianionic disubstituted guanidine - (*N*-carboxymethylguanidino) hydroxyacetic acid-$C_5H_6N_3O_5$ - oag^{3-}, is the derivative ligand formed *in situ* (Fig. 5a) [21]. In this complex, oag is coordinated with two copper(II) ions through three oxygen atoms and one nitrogen atom, whereas GAA has coordinated with both copper(II) ions through two oxygen atoms from a carboxylate-bridged group. Fig. 5b shows the simplified mechanism of the oag formation [21].

There is also a nickel(II) complex with GAA and aspartic acid (ASP), $[Ni(Asp)(GAA)]H_2O$, where the trans Ni–N and Ni–O coordination was observed [22].

Besides copper and nickel, the investigation and understanding of GAA coordination with zinc may be of great interest since it is essential to our organism, and is present in essential biological molecules, such as important enzymes like Zn-Cu-superoxide dismutase [23], carbonic anhydride [24], carboxypeptidase, alcohol dehydrogenase, as well as the DNA-related compounds, the zinc-fingers [25]. In addition, zinc plays a vital role in maintaining essential body functions related to immunity, brain function, tissue growth, and insulin metabolism [26]. It has also been investigated for the potential use of its complexes with amino acids in dermatology [27].

Zinc coordination with several amino acids has already been studied, and many complexes were synthesized [28], but the zinc monocrystal complex with GAA was not reported yet. In this study, we present a new ZnGAA complex that has been only synthesized with success in the presence of Cu(II) salt and for this reason, we also make comparisons with copper(II) complexes with GAA already obtained.

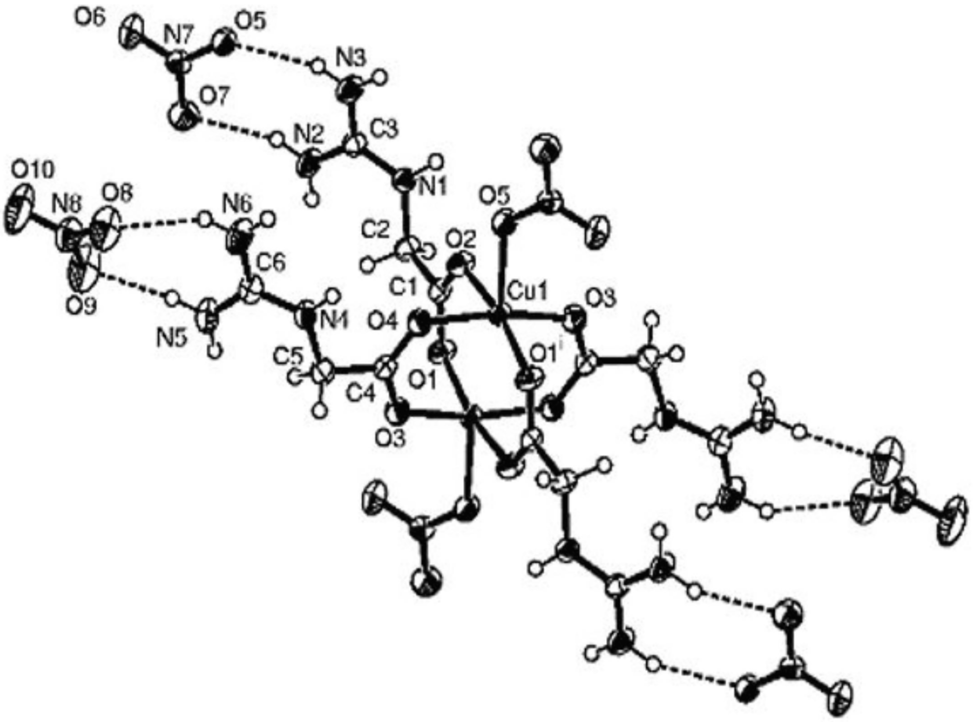

Fig. 3. Structure of $Cu_2(GAA)_4(NO_3)_2$ (tetrakis(μ-guanidinoacetic acid-κ2O:O′) bis[(nitrato-κO) copper(II)]) (own authorship).

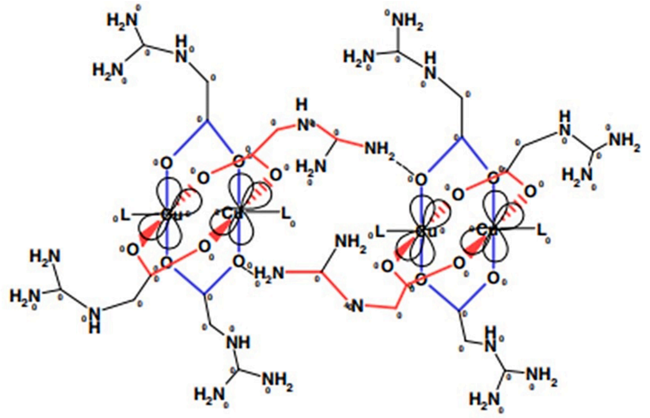

Fig. 4. Sketch of a paddlewheel copper dimer, $Cu_2(GAA)_4(NO_3)_2$ showing the d orbitals of Cu(II) involved, based on single-crystal X-ray diffraction and electron paramagnetic resonance studies, L = NO_3 [Reproduced with permission of 20].

2. Experimental section

2.1. *Synthesis of the guanidinoacetic complex with Zn - (HGAA)[Zn(GAA)Cl_3]·H_2O*

The complex (HGAA)[Zn(GAA)Cl_3]·H_2O was synthesized by reacting 0.1 mol of an aqueous solution of guanidinoacetic acid (Aldrich Chemical Co. Inc.) with 0.1 mol of $ZnCl_2$ (Merck) in the presence of 0.01 mol of $Cu(NO_3)_2$ (Merck). The obtained solution was homogenized (pH range 3.0–4.0) and left to stand at room temperature. Transparent crystals were formed at a very low yield. Thus, (HGAA)[Zn(GAA)Cl_3]·H_2O monocrystals formed only in the presence of copper(II) solution.

It is interesting to notice that previous unsuccessful attempts to synthesize crystals of the Zn(II) complex of GAA have been done with different procedures using Zn(II) salts at different pH values. For example, we have prior synthesized a zinc complex with GAA with the addition of a basic solution for pH adjustment but it was only obtained in the powder solid form [29].

2.2. *Characterization of complex (HGAA)[Zn(GAA)Cl_3]·H_2O*

This complex was analyzed using the following techniques:

Single-Crystal X-ray Diffraction Analysis - A single crystal of the complex was chosen and mounted on an Enraf-Nonius Kappa CCD diffractometer with graphite monochromated Mo Kα (λ = 0.71073 Å) radiation. Unit cell parameters were based on all reflections. Data collection was carried out using the COLLECT program [30]; integration and scaling of the reflections were performed with the HKL Denzo-Scalepack suite of programs [31]. The structure was determined by direct methods with SHELXS-97 [32]. The model was refined by full-matrix least squares based on F^2, through SHELXL-97 [32]. Hydrogen atoms were stereo-chemically positioned and refined with the ridging model. Their isotropic displacement parameters were set to 20 % greater than the equivalent isotropic displacement parameter of the atom to which each one is bonded. Exceptions are hydrogen atoms bonded to water oxygen and to nitrogen atoms N1 and N4. These hydrogen atoms were found on the Fourier difference maps, and their positions and isotropic displacement parameters were fixed. Non-hydrogen atoms were anisotropically refined. Relevant experimental features are shown in Table 1.

Fourier transform infrared spectroscopy - Infrared spectra were recorded using CsI pellets in the mid-region (4000–500 cm^{-1}) and far-region (600–150 cm^{-1}) with 16 scans on a Nicolet 6700 FT-IR Infrared spectrometer.

Elemental Analysis - CHN elemental analysis has been done in a Perkin-Elmer 2400 CHN Elemental Analyzer. The obtained results were the following: calculated (found): C 16.95 % (16.75 %), H 4.00 % (3.60 %), and N 19.78 % (19.50 %). Unfortunately, due to the small sample quantity, neither zinc analysis nor oxygen could be done.

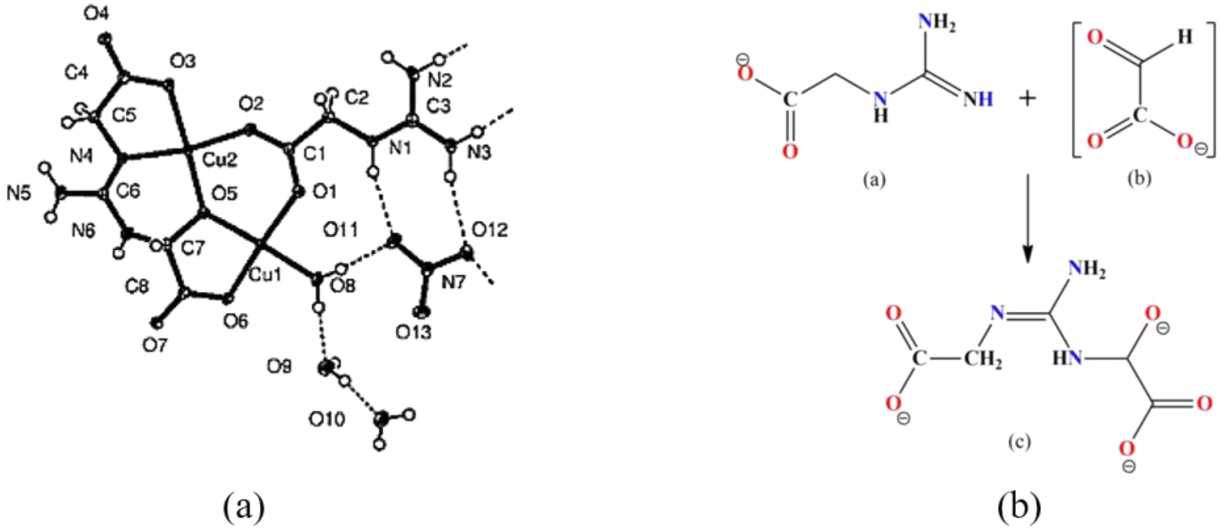

Fig. 5. (a) Crystal structure of $[Cu_2(oag)(Gaa)(H_2O)]$ NO_3 $2H_2O$, where oag (*N*-carboxymethylguanidino)hydroxyacetic acid-$C_5H_6N_3O_5$, oag^{3-}) is derivative ligand formed *in situ* [Reproduced with permission of 21]. (b) Simplified mechanism of the oag formation: (a) guanidinoacetate, (b) fragment of desamidination of GAA, and (c) oag structure (own authorship).

Table 1
Crystal data and structure refinement for $(HGAA)[Zn(GAA)Cl_3]^{\cdot}H_2O$.

Empirical formula	$ZnC_6H_{18}N_6O_5Cl_3$
Formula weight	424.75 g.mol $^{-1}$
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 10.0056(4) Å
	b = 11.2145(7) Å
	c = 14.6932(8) Å
	β = 96.355(3) Å
Volume	1638.56(15) Å^3
Z	2
Density (calculated)	1.957 mg.m^{-3}
Absorption coefficient	2.015 mm^{-1}
F(0 0 0)	864
Crystal size	0.07 × 0.10 × 0.15 mm^3
Theta range for data collection	3.25–26.5°
Index ranges	$-12\leq h\leq 12$, $-14\leq k\leq 12$, $-18\leq l\leq 18$
Reflections collected	5805
Independent reflections	3446 [R(int) = 0.0514]
Completeness to theta = 26.50°	99.1 %
Absorption correction	None
Max. and min. transmission	0.92 and 0.87
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3446/0/190
Goodness-of-fit on F^2	0.911
Final R indices [I > 2sigma(I)]	R1 = 0.0450, w$R2$ = 0.0976
R indices (all data)	R1 = 0.1038, w$R2$ = 0.11161
Largest diff. peak and hole	0.375 and −0.660 e.Å^{-3}

2.3. Speciation analysis in aqueous solution

Speciation of GAA as well as Zn(II) and Cu(II) complexes as a function of pH have been done employing the Hyss Program [33,34]. The input data of stability constants were beforehand determined [18]. The concentrations of GAA, Cu(II), and Zn(II) used for this speciation determination were similar to those employed for the synthesis of the $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ complex.

3. Results and discussion

3.1. The complex of guanidinoacetate with zinc-crystal structure analysis

The crystal structure was determined by X-ray diffraction. The compound crystallizes in the space group $P2_1/c$. Data collection parameters and refinement results are shown in Table 1.

The asymmetric unit of the crystal is composed of one unit of $[Zn(GAA)Cl_3]^-$, trichloro-*O*-guanidinoacetate-zinc(II), one molecule of water, and one unit of protonated guanidinoacetic acid $HGAA^+$. The zinc atom is bonded to one carboxylate oxygen and three chloride ions in a tetrahedral coordination (Fig. 6a and 6b). Table 2 shows selected bond lengths (Å) and angles (°) for $(HGAA)[Zn(GAA)Cl_3]^{\cdot}H_2O$. As expected for normal Zn–Cl bonds, the Zn–Cl bond distances are in the range of 2.26 Å – 2.28 Å whereas Zn-O bond from carboxylate group of GAA, Zn(1)–O(1), is 1.970 Å (Table 2). Geometric parameters show the electron delocalization of the carboxylate group of GAA, O(1)-C(1)-O(2), which is bonded to the zinc atom: bonds C(1) O(1) (1.273(5)Å) and C(1) O(2) (1.239(5)Å) are close to each other. By contrast, the carboxylic acid group of the non-coordinated $HGAA^+$ has one double bond (C(4)-O(4), 1.217(5)Å) and one single bond (C(4)-O(3), 1.297(5)Å).

The complex $(HGAA)[Zn(GAA)Cl_3]$ is stabilized by hydrogen bonds involving the water molecule, which plays a fundamental role in linking the isolated guanidinoacetic acid to the guanidinoacetate unity, which is coordinated to the zinc(II) metal ion, as well as to three chloride ions (Fig. 6a). The tetrahedrally coordinated zinc atom is thus bonded to three chloride ions and one guanidinoacetate unit (through one carboxylic oxygen), as depicted in Fig. 6b. Two chloride ions (Cl1 and Cl3) lie approximately on the plane formed by the zinc atom and the guanidinoacetate. Chloride Cl2, which forms a Zn–Cl bond approximately perpendicular to the guanidinoacetate plane, is hydrogen-bonded to water. The structure is formed by parallel layers linked through the water hydrogen bonds and the Zn1–Cl2 bonds: as shown in Fig. 6b, each chloride Cl2 is hydrogen-bonded to two guanidinoacetate units (through hydrogen bonds N3–HN3b — Cl2 and N5–HN5a — Cl2) and one water molecule (through bond Ow–HOw2 — Cl2).

Fig. 7a shows the [104] crystallographic direction in the complex, where the crystal structure consists of parallel hydrogen-bonded layers. The water molecules play a fundamental role in stabilizing the crystal structure connecting neighboring GAA groups through N5–H — Ow and O3–H — Ow hydrogen bonds (Fig. 7b). Beyond this, neighboring layers

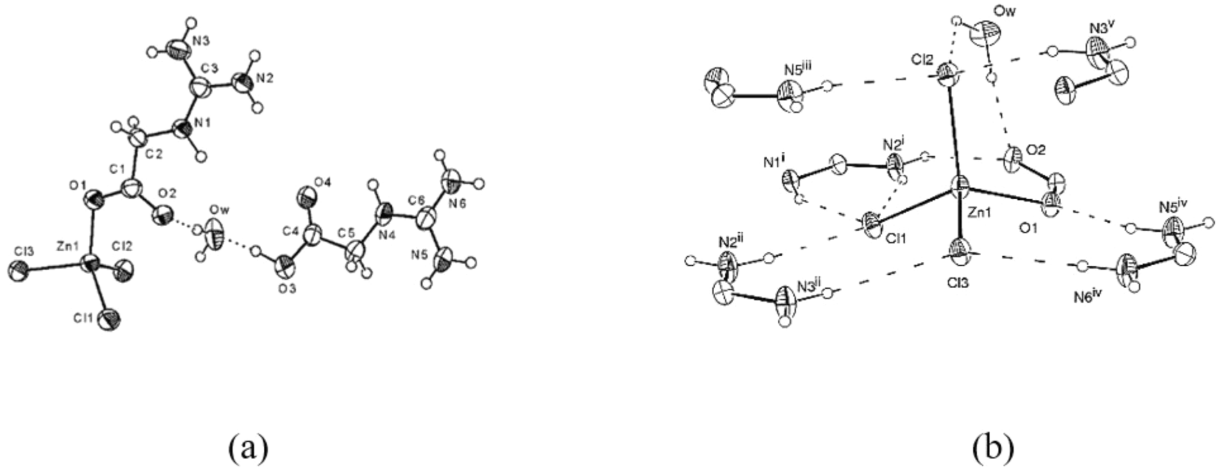

Fig. 6. Coordination of zinc and hydrogen bonds of bonded atoms in (HGAA)[Zn(GAA)Cl_3]·H_2O: (a) Ellipsoid probability set to 20 %. (b) Ortep drawing of the asymmetric unit of the title compound. Displacement ellipsoids at 20 % probability level. Hydrogen bonds are represented as dashed lines.

Table 2
Selected bond lengths (Å) and angles (°) for (HGAA)[Zn(GAA)Cl_3]·H_2O.

Zn(1)–O(1) 1.970(3) O(1)-C(1) 1.273(5) O(2)-C(1) 1.239(5) C(1)-C(2) 1.499(6)	Zn(1)-Cl(1) 2.2642(11) N(1)-C(2) 1.454(5) N(1)-C(3) 1.313(5) N(2)-C(3) 1.327(5) N(3)-C(3) 1.324(5)	Zn(1)-Cl(2) 2.2744(12) O(3)-C(4) 1.297(5) O(4)-C(4) 1.217(5) C(4)-C(5) 1.509(5)	Zn(1)-Cl(3) 2.276(12) N(4)-C(5) 1.432(6) N(4)-C(6) 1.335(5) N(5)-C(6) 1.322(5) N(6)-C(6) 1.317(6)
O(1)-Zn(1)-Cl(1) 117.34(9) O(1)-Zn(1)-Cl(2) 110.18(9)	Cl(1)-Zn(1)-Cl(2) 111.39(5) O(1)-Zn(1)-Cl(3) 101.74(9)		Cl(1)-Zn(1)-Cl(3) 105.39(4) Cl(2)-Zn(1)-Cl(3) 110.09(4)

interact via hydrogen bonds involving water molecules (Fig. 8): parallel layers of molecules are connected through medium-strength hydrogen bonds involving the water molecules, Ow–HOw1…O2 (d[O—O] = 2.761(5) Å) and Ow–HOw2 — Cl2 (d[O–Cl] = 3.297(3) Å). Therefore, hydrogen bonds play a crucial role in stabilizing the crystal structure, connecting neighboring molecule layers or molecules within each layer.

The water links, via hydrogen bonds Ow–HOw1…O2 and O3–HO3…Ow (Fig. 7, Table 3), the [Zn(GAA)Cl_3]$^-$ unit to the $HGAA^+$ unit. (Fig. 8, Table 3).

3.2. *Fourier transform infrared analysis (FTIR)*

Fig. 9a and Fig. 9b present the infrared spectra of both guanidinoacetic acid and the zinc complex, (HGAA)[Zn(GAA)Cl_3]·H_2O, in the mid (4000–500 cm^{-1}) and far region (600–150 cm^{-1}).

The guanidinoacetic acid mid-infrared spectrum (Fig. 9a) shows the following main bands: ν(N—H) of the guanidino group at 3390 cm^{-1}, relative to ν_s and ν_a of primary amines in the 3000–3200 cm^{-1} region, ν(C=N) of the guanidino group at 1670–1630 cm^{-1} and ν_a and ν_s of the carboxylate group at 1590 and 1410 cm^{-1}, respectively. All these data are in good agreement with literature values [35].

In an overview for comparison between guanidinoacetic acid and zinc complex mid-infrared spectra (Fig. 9a), it can be observed a great similarity between them. This indicates a very slight change in the amino acid structure after its complexation with zinc, congruent with the mono-oxygen carboxylate coordination. A slight shift in the band of

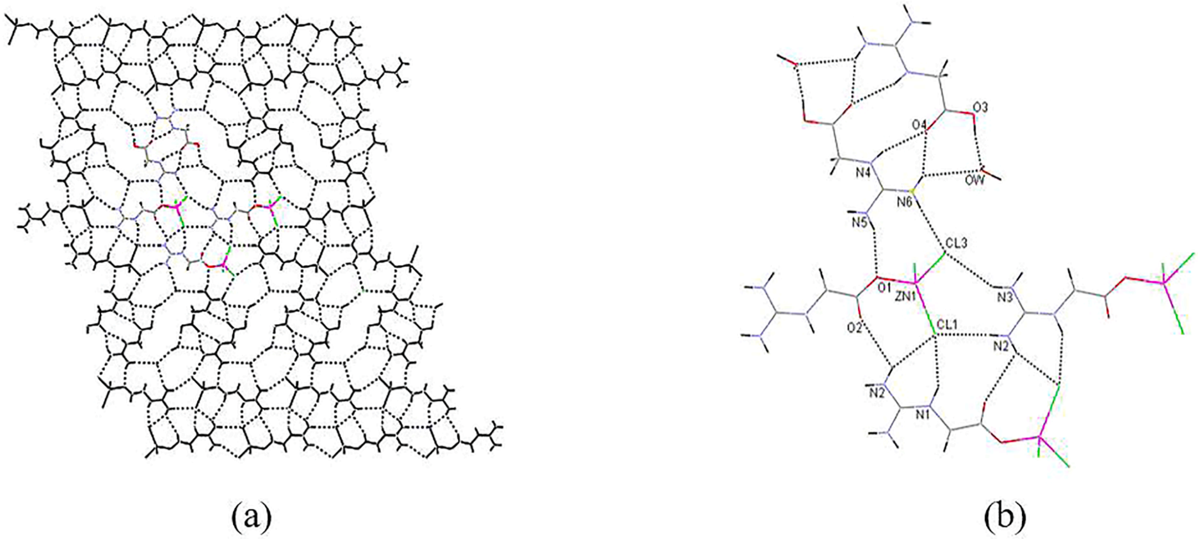

Fig. 7. Hydrogen bonds in (HGAA)[Zn(GAA)Cl_3]·H_2O. (a) Hydrogen bonds (dashed); and (b) hydrogen bonds network of one layer of molecules in direction [104]. Hydrogen bonds are represented as dashed lines.

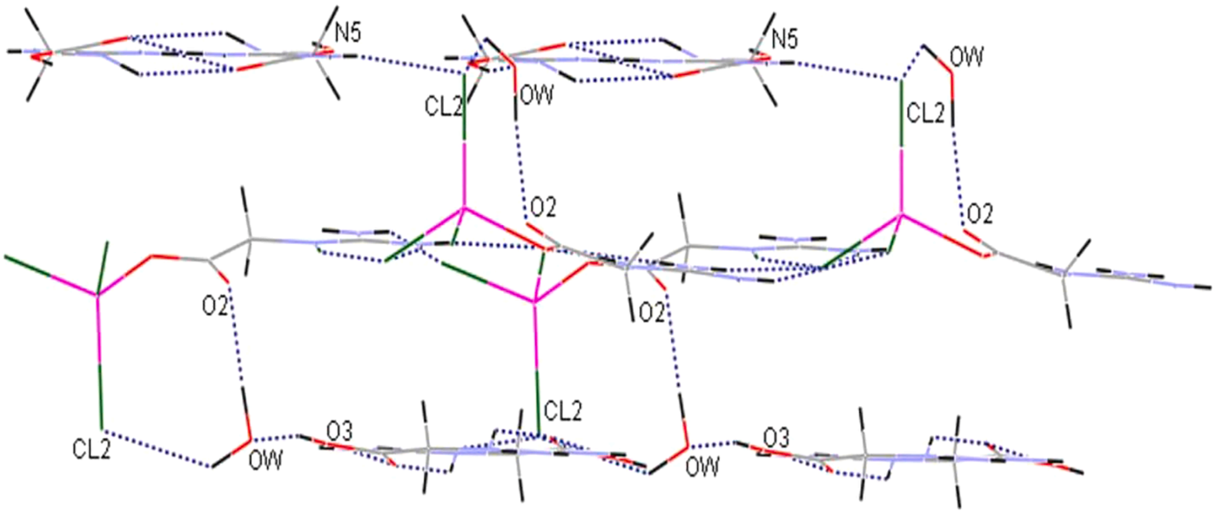

Fig. 8. Representation of three parallel layers of molecules in a crystal of $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ showing the importance of Ow–HOw1 — O2 and Ow–HOw2 — Cl2 interactions in connecting these layers.

Table 3
Hydrogen bond parameters crystal of $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$.

A – H···B	d[A – B] (Å)	d[A-H] (Å)	d[H···B] (Å)	<[A–H–B] (°)
N1-HN1A···Cl1^{i}	3.417(3)	1.005(3)	2.4850(11)	153.9(2)
N2-HN2A···O2^{i}	3.033(5)	0.86	2.53	117.9
N2-HN2A···Cl1^{i}	3.351(4)	0.86	2.55	155.6
N2-HN2B···Cl1^{ii}	3.294(4)	0.86	2.44	174.1
N3-HN3B···Cl2^{iii}	3.331(4)	0.86	2.52	156.8
N3-HN3A···Cl3^{ii}	3.316(4)	0.86	2.55	148.8
N4-HN4A···O4^{vi}	2.967(5)	0.936(4)	2.145(3)	146.0(2)
N5-HN5B···O1^{iv}	3.037(5)	0.86	2.22	158.1
N5-HN5A···Cl2^{v}	3.450(4)	0.86	2.61	167.2
N6-HN6A···Cl3^{iv}	3.253(4)	0.86	2.39	176.3
N6-HN6B···O4^{vi}	2.959(5)	0.86	2.19	149.2
N6-HN6B…Ow^{vi}	3.276(6)	0.86	2.67	128.3
Ow-HOw1···O2	2.761(5)	0.947(3)	1.817(3)	174.2(3)
Ow-HOw2···Cl2	3.297(3)	1.009(4)	2.5809(11)	127.80(19)
O3-HO3···Ow	2.607(5)	1.061(3)	1.561(3)	167.6(2)

Symmetry operations: (i) [-x + 1, y + 1/2, -z + 1/2]; (ii) [x, y + 1, z]: (iii) [-x + 2, y + 1/2, -z + 1/2]; (iv) [x-1, -y + 1/2, z + 1/2]; (v) [-x + 1, -y, -z + 1]; (vi) [-x + 1, -y + 1, -z + 1].

ν_s of the carboxylate group can be observed, shifted from 1590 to 1596 cm^{-1}, resulting from electron delocalization of the carboxylate group of GAA, O1-C1-O2 due to zinc coordination, according to Fig. 6a.

In the 600–150 cm^{-1} region of infrared spectra for guanidinoacetic acid and $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ complex (Fig. 9b), new bands can be observed at 551, 412, 293, 273, and 237 cm^{-1}. The band at 551 cm^{-1} may be attributed to the water deformation band, probably attached to other units by hydrogen bonds or coupled with ν(Zn-O). The band at

Table 4
Stability Constants of GAA Complexes with Cu(II) and Zn(II) [Reproduced with permission of 38].

Log K Metal Ion					
p	q	r	1/H$^+$	Cu(II)	Zn(II)
0	1	1	2.90 ± 0.04	–	–
0	1	2	10.91 ± 0.07	–	–
0	1	1	2.59*	–	–
0	1	2	10.85*	–	–
1	1	0	–	7.69 ± 0.07	7.39 ± 0.06
1	1	−1	–	1.04 ± 0.05	–
2	2	−2	–	3.77 ± 0.11	6.45 ± 0.10

p: metal ion; q: ligands; r: hydrogen ion - * Data from Ref. [39].

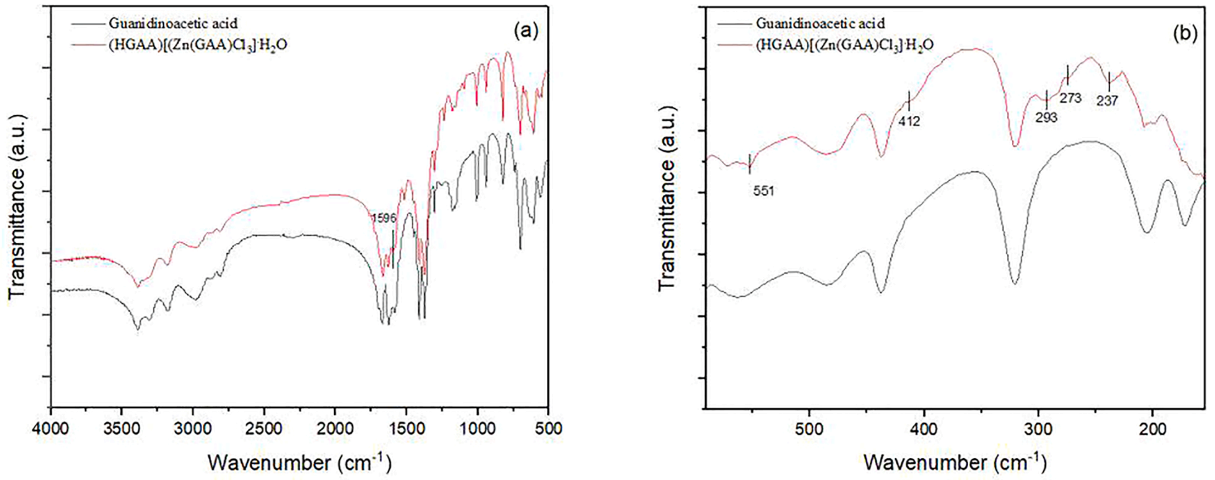

Fig. 9. Infrared spectra of guanidinoacetic acid and $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ complex: (a) 4000–500 cm^{-1} infrared region; and (b) 600–150 cm^{-1} infrared region.

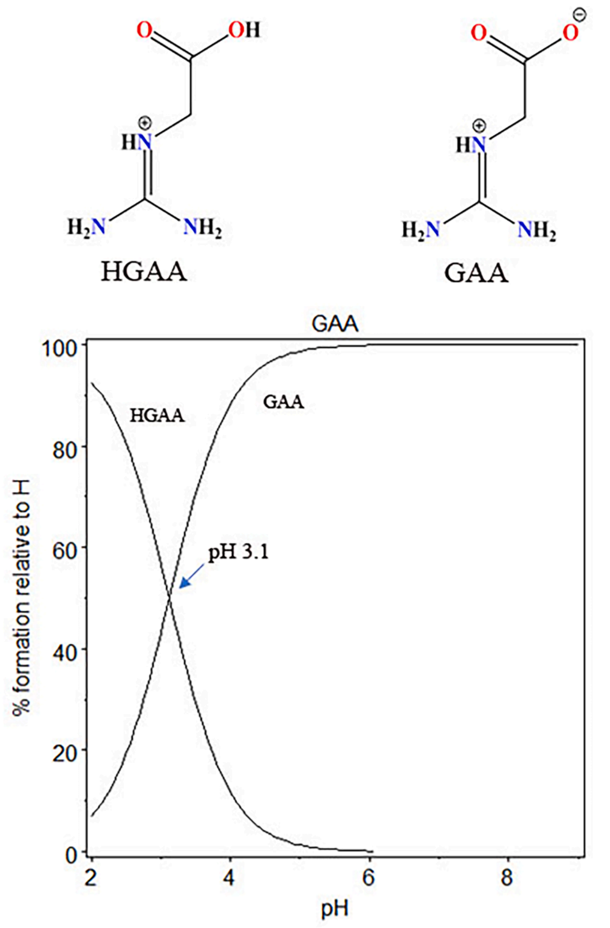

Fig. 10. Speciation of guanidinoacetic acid as a function of pH, employing the Hyss Program [34].

412 cm^{-1} is probably related to ν(Zn-O), in agreement with Zn(II) complexes with other amino acids such as glycine, alanine, valine, leucine, isoleucine, and phenylalanine [36]. The bands at 293 cm^{-1}, 273 cm^{-1}, and 237 cm^{-1} probably correspond to ν Zn-Cl [36] of the three coordinated chloride ions (Fig. 6a).

3.4. Stability of GAA complexation with Zn and Cu(II) – Comparative analysis

In order to try to elucidate the role of Cu(II) in the synthesis of the $[Zn(GAA)Cl_3]^-$ - trichloro-*O*-guanidinoacetate-zinc(II) complex (see Experimental section), a comparative analysis between Cu(II) and Zn(II) and their competition for GAA coordination was performed.

It is interesting to observe that a zinc complex with GAA has been previously synthesized, $Zn(HGAA)NO_3Cl$, but only in powder and with an oxygen-GAA coordination, a bridging nitrate, and chloride ions as ligands [29].

Table 4 shows the stability constants of Cu(II) and Zn(II) complexes with GAA calculated by Felcman and Miranda [18,37,38]. GAA has two protonation sites that can be detected experimentally by potentiometric analysis, namely: pK_{a1} related to the carboxylic group; and pK_{a2} corresponding to the alpha-amino group, since the terminal nitrogen amino groups are very basic [18,38,39,40]. Fig. 10 shows the speciation of GAA as a function of pH.

From Table 4, it can be observed that log β of ML for Cu(II) and Zn(II) in an aqueous medium are very close, 7.69 and 7.39 [38,39], indicating a tight competition between them, in opposition to the greater stability for Cu(II) complexes according to the expected by Irwing-Williams series.

The species distribution diagram as a function of pH using GAA percentage was done, using data for the Cu(II) and Zn(II) complexes from Table 4 and employing Hyss Program [33,34] (Fig. 11a and b). The concentrations of Zn(II), Cu(II), and GAA were the same used in the synthesis methodology.

Making comparisons with the formation of complexes in an aqueous medium for Cu(II) and Zn(II) equilibria in the presence of GAA, it can be observed a predominance of ZnGAA complex over CuGAA complex. The presence of Cu(II) also may contribute to the predominance of $HGAA^+$ species in the equilibrium in the same pH range 3.0–4.0 of the synthesis

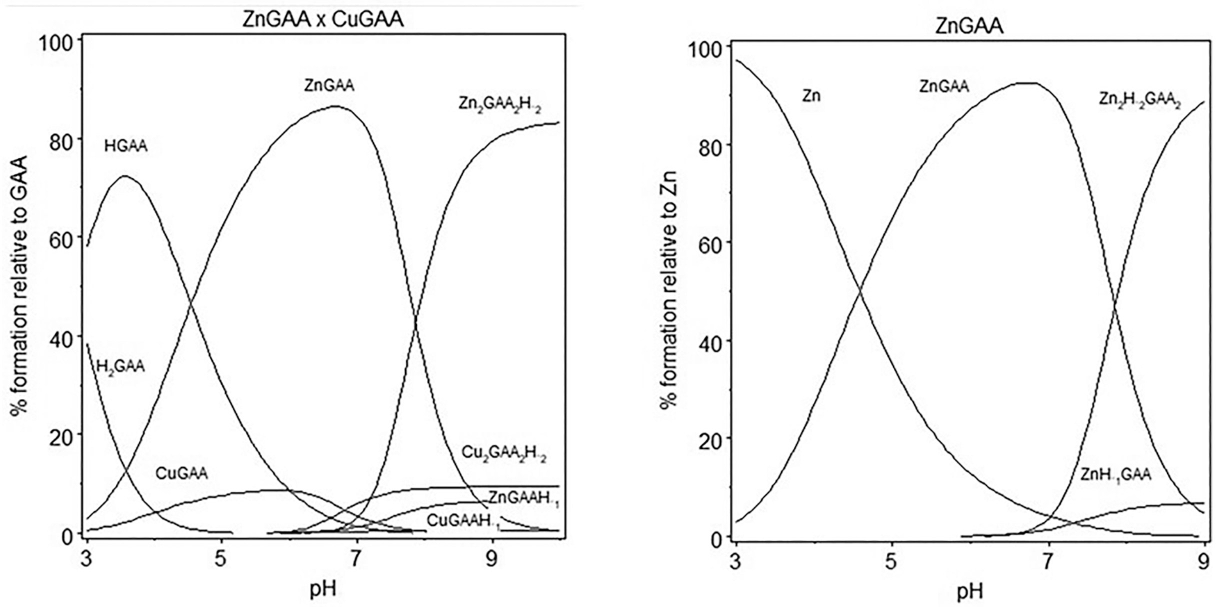

Fig. 11. (a) Distribution of species as a function of pH for Zn(II) and Cu(II) complexes with GAA, where HGAA is guanidinoacetic acid protonated at oxygen carboxylate group, GAA is the zwritten ion, H_2GAA is a diprotonated species, and H^{-1} is OH^-. (b) Distribution of species as a function of pH for Zn:GAA system, employing the Hyss Program [34].

of $(HGAA)[Zn(GAA)Cl_3]\cdot H_2O$ complex. The $HGAA^+$ species played a fundamental role in the charge stabilization of the synthesized complex in addition to the hydrogen bonds between them and a water molecule (Fig. 6a).

4. Conclusions

This study reported a novel crystal of the Zn(II) complex with guanidinoacetate ion from guanidinoacetic acid that could only be synthesized in the presence of Cu(II) solution, probably due to its influence in the equilibrium and speciation as a function of pH involving this amino acid.

According to crystal structure analysis, the zinc complex, trichloro-*O*-guanidinoacetate-zinc(II) exhibited a tetrahedral geometry that crystallizes in the space group $P2_1/c$, where the guanidinoacetate was coordinated in a monodentate mode through its oxygen atom from a carboxylate group, complemented by three chloride ligands. It is important to notice that intermolecular hydrogen bonds play an important role in the stabilization of the complex as it was observed between the zinc complex, a molecule of water, and a neighboring protonated guanidinoacetic acid. In addition, the infrared spectroscopy analyses corroborated the oxygen-monocoordination of guanidinoacetate with zinc in the complex.

The different coordination modes of guanidinoacetate ion and its complexation with zinc and copper(II), as well as the way they stabilize their structures, may help to further understand the diverse biochemical processes involved in this amino acid.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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