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Synthesis and structure investigation of the antibiotic amoxicillin complexes of d-block elements

M.A. Zayed[a,*], S.M. Abdallah[b]

[a] *Chemistry Department, Faculty of Science, Cairo University, Giza, Egypt*
[b] *El-gamma El-Omalia, Cairo, Egypt*

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Abstract

The study of some transition metals (M) and amoxicillin trihydrate (ACT) ligand complexes (M–ACT) that formed in solution involved the spectrophotometric determination of stoichiometric ratios and their stability constants and these ratios were found to be M:ACT = 1:1, 1:2 and 2:1 in some instances. The calculated stability constants of these chelates, under selected optimum conditions, using molar ratio method have values ranging from $K_f = 10^7$ to 10^{14}. These data were confirmed by calculations of their free energy of formation ΔG, which corresponded to their high stabilities. The separated solid complexes were studied using elemental analyses, IR, reflectance spectra, magnetic measurements, mass spectra and thermal analyses (TGA and DTA). The proposed general formulae of these complexes were found to be $ML(H_2O)_w(H_2O)_x(OH)_y(Cl)_z$, where M = Fe(II), Co(III), $w = 0$, $x = 2$, $y = 1$, $z = 0$; M = Co(II), $w = 0$, $x = 1$, $y = 0$, $z = 1$; M = Fe(III), $w = 0$, $x = 1$, $y = 2$, $z = 0$; M = Ni(II), Cu(II) and Zn(II), $w = 2$, $x = 0$, $y = 1$, $z = 0$, where w = water of crystallization, x = coordinated water, y = coordinated OH^- and $z = Cl^-$ in the outer sphere of the complex. The IR spectra show a shift of ν(NH) (2968 cm^{-1}) to 2984–2999 cm^{-1} of imino group of the ligand ACT and the absence of ν(CO) (β-lactame) band at 1774 cm^{-1} and the appearance of the band at 1605–1523 cm^{-1} in all complexes suggest that 6,7-enolization takes place before coordination of the ligand to the metal ions. The bands of M—N (at 625–520 cm^{-1}) and of M—O (at 889–7550 cm^{-1}) proved the bond of N (of amino and imino groups) and O of C—O group of the ligand to the metal ions. The reflectance spectra and room temperature magnetic measurements refer to octahedral complexes of Fe(II) and Fe(III); square planner form of Co(II), reduced Co(III), Ni(II) and Cu(II)–ACT complexes but tetrahedral form of Zn–ACT complex. The thermal degradation of these complexes is confirmed by their mass spectral fragmentation. These data confirmed the proposed structural and general formulae of these complexes.

Keywords: Synthesis; ACT–M complexes; Spectroscopic measurements; Thermal analyses

1. Introduction

Amoxicillin trihydrate (Fig. 1) is a white odorless crystalline powder. It is the 4-hydroxy analogue of ampicillin and used against a similar variety of infections although it should not be used in shigellosis. It had been used as an alternative to chloramphenicol in the treatment of infections caused by salmonella. It is usually given by mouth, as the trihydrate. The usual dose is 250–500 mg three times daily. It may be given by injection for moderate infections but in severe ones, 1 g may be given every 6 h [1].

The mechanism of the colour reaction between ACT and Cu salts together with biuret reagent to form mixed-ligand copper complexes, in the molar ratio 1:1 [2] had been studied. Spectrometric studies of this reaction had been used to determine ACT in pharmaceuticals at λ = 750, 650 and 640 nm [3]. Several physico-chemical studies of the complexation reaction of the sodium salt of amoxicillin and Cu(II) were performed by spectrophotometeric analysis. The data obtained demonstrated the formation of 1:1, 1:2 and 2:1 complexes [4].

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[*] Corresponding author. Present address: Chemistry Department, Faculty of Education for Girls, Elmontazah, Elgarbi, P.O. Box 1921, Borida, ElQasseem 9114, Saudi Arabia. Tel.: +966 63850783; fax: +966 63850783.
E-mail addresses: mazayed429@hotmail.com, mazayed429@yahoo.com (M.A. Zayed).

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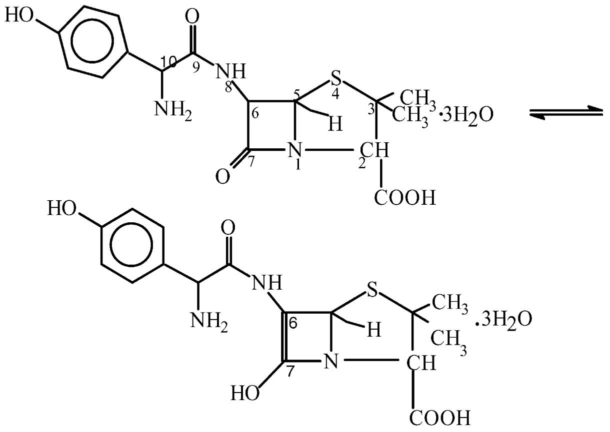

Fig. 1. Amoxicillin trihydrate (ACT) 6,7-keto-enol forms.

The dc and differential pulse polarographic measurements were used to study the behavior of Ni(II)–ampecillin and Ni(II)–ACT complexes at the dropping mercury electrode [5,6]. The spectrophotometric method used for the study of the formation of Ni(II)–ACT in capsules was used for the microdetermination of this drug [7].

The effects of pH, temperature and ion concentrations on the hydrolysis kinetics of amoxicillin (AC) catalyzed by Cu(II), V(IV) and V(V) ions were studied via the formation of the binary complexes of these metals [8].

The present research work aims chiefly to shed more light on the chemical behavior of some life-essential drugs such as amoxicillin trihydrate (ACT). ACT has essential biological roles in curing different kinds of diseases. It takes several pathways in the human body and interacts in vivo systems in aqueous media. Consequently, it is important to manipulate its chemical interaction with some important transition metal cations of vital biological roles in the human body. It involved a study of ACT–3d-block elements complexes both in solution and in the solid state. The synthesized solid complexes were subjected to very careful inspection by elemental, spectroscopic and thermal analyses.

2. Experimental

All chemicals used in this study were of analytical grade. They included ACT of the formula $C_{16}H_{19}N_3O_5S\cdot3H_2O$, and the metal salts $FeSO_4\cdot6H_2O$, $Fe_2(SO_4)_3$, $Co(NO_3)_2\cdot6H_2O$, $Na_3[Co(NO_2)_6]$, $NiSO_4\cdot7H_2O$, $CuCl_2$ and $ZnSO_4\cdot7H_2O$. These chemicals were purchased from Merck or Aldrich. The organic solvents, methanol (98%), ethanol (95%), *N*-pentane (98%) and acetone (97%) were purchased from BDH and used without further purification.

2.1. Preparation of solid complexes

The solid M–ACT complexes were prepared by dropwise addition of 25 mL of a 0.01 M metal salt solution (10 mmol) to 25 mL of a 0.01 M ACT (4.19 g L^{-1}, 10 mmol) solution with continuous stirring at room temperature and at pH values 8.2–8.8 adjusted by solutions of 0.1 M NaOH or 0.1 M Na_2CO_3 using a pH-meter. The mixtures were refluxed in a 100 mL rounded-bottom flask for 1–2 h. The solid precipitates obtained were filtered in a Hirsch funnel, washed with hot water and *N*-pentane several times and dried in an oven at 80 °C. The solids obtained were crystallized from an ethanol–water mixture (1:1), dried and analyzed by microanalyses at the Microanalytical Center of Cairo University. The complexes were investigated by the various physicochemical methods previously mentioned.

2.2. Solutions

A 10^{-3} M ACT solution was prepared by dissolving the appropriate amount (0.419 g) of the ligand in 1 L bidistilled water. A 10^{-3} M solutions of Fe(II), Fe(III), Co(II), Co(III), Ni(II), Cu(II) and Zn(II) cations were prepared by dissolving the appropriate weights of the metal salts mentioned previously in bidistilled water.

2.3. Instruments and apparatus

The UV and visible spectra of the ligand and complexes in solution were measured by a recording 240 Shimadzu UV–vis or a manual Spectronic 601spectrophotometer at room and various temperatures using 1 cm matched silica cells. The pH-meters used for pH adjustment were a model 28 Radiometer pH-meter, a model 87 digital pH/mV-Messgeräte or a model 701A pH/mV-Ionanalyzer. The various temperatures of reactions in the solution vessels were adjusted by using a HAAKF Model NB22 ultrathermostat. The IR spectra of the solid ligand and complexes as KBr disks were measured using a Perkin-Elmer 1430 spectrophotometer in the wave number range 400–4000 cm^{-1}. The UV–vis reflectance spectra of the solids were measured using a model 3101 Shimadzu PC spectrophotometer and $BaSO_4$ background. The thermal analyses (TG, DTG, and DTA) were carried out using TGA-5OH and DTA-5OH Shimadzu thermal analyzers respectively with a heating rate 10 min^{-1} in nitrogen atmosphere.

2.4. Selected suitable conditions for complex formation in solution

The reactions of the various metal ions such as Fe(II), Fe(III), Co(II), Co(III), Ni(II), Cu(II) and Zn(II) ions with ACT were studied spectrophotometrically under various experimental conditions to select the optimum ones. The effect of pH on the spectra of the various complexes were studied by placing of 1.0 mL of a 10^{-3} M ACT solution in a 5 mL measuring flask and addition of a series of universal buffers of pH 1.91–12.40 and measuring absorbency at λ ranging between 330 and 390 nm. The effect of *N*-bromosucinimide (NBS) as oxidant and the effect of temperature on the complex formation of ACT–3d-block series were studied.

2.5. The stoichiometry of d-block element–ACT complexes

The stoichiometric ratio between 3d-block elements [M] and the drug ligand (ACT) was studied by the molar ratio method (mrm) in which [ACT] was varied from 0.1×10^{-3} to 1.0×10^{-3} M in a mixture with constant $[M] = 1 \times 10^{-3}$ M, $NaNO_2$, *N*-bromosuccinimide (NBS) and a buffer of suitable pH. The absorbency of solutions was measured at selected λ_{max} and plotting absorbency against [ACT]/[M], the inflection points gave ratio values of 1:1 and 1:2 (M:ACT).

2.6. Evaluation of the stability formation constant K_f and free energy change (ΔG) of the formed complexes

The extent to which complex formation occurs is usually expressed by a formation constant, K_f, of a complex at particular conditions. These conditions are (pH = 7.71–8.80, λ_{max} = 325, 255, 320, 255, 260, and 265 nm for Fe(II)–ACT, Fe(III)–ACT, Co(II)–ACT, Co(III)–ACT, Ni(II)–ACT, and Cu(II)–ACT, respectively, at room temperature and developing time of 5–10 min). Spectrophotometric results obtained under the practical selected optimum conditions were used for the calculation of K_f and ΔG of the M–ACT chelates.

3. Results and discussion

In view of the vital role of amoxicillin as drug (given orally to humans or as injection) it is very important to study its interaction with transition metals that normally are present in vivo system. This study involves two stages, in solution and in the solid state in order to explain their possible interactions in vivo systems [9]. Applying the recommended molar ratio method (mrm) [10], the study of the formation of M–ACT complexes under selected optimum conditions in all cases, it shows straight lines intersecting at [ACT]:[M] ratios of 1:1 and 1:2.

The extent, to which these complexes are formed, is usually expressed by the formation constant K_f (apparent conditional stability constant) at particular pH, λ_{max} and temperature. This pH is usually calculated from the expression K_f/α where α is the fraction of ligand attached to the metal cation. This stability is also expressed by the free energy change (ΔG) of these complexes, applying the molar ratio method

Table 1
The apparent formation (conditional) constant (K_f), and free energy change (ΔG) for ACT–transition metal complexes by using molar ratio method (mrm) at pH = 7.71–8.80, at ambient temperature (25 °C), developing time = 5–10 min and corresponding λ_{max} (nm)

Compound	λ_{max}	Ratio	A	A_m	$A - A_m$	$1 - (A/A_m)$	K_f	ΔG (25 °C) (kcal mol deg^{-1})
$[FeL(OH)(H_2O)_2]$ (formula weight = 475)	325	1:1	0.72	0.76	0.947	0.0526	1×10^7	9.608
		1:2	1.08	1.12	0.964	0.0357	2.604×10^{13}	18.414
		1:1	0.75	0.78	0.961	0.0348	1×10^7	9.608
		1:2	1.22	1.25	0.976	0.0240	6.23×10^{13}	18.934
$[Fe(OH)_2L(H_2O)]$ (formula weight = 474)	255	1:1	2.42	2.45	0.987	0.0122	4.083×10^7	10.446
		1:2	2.58	2.60	0.992	0.0076	17.187×10^{14}	20.911
	350	1:1	0.80	0.82	0.975	0.0243	1.796×10^7	9.957
		1:2	1.18	1.22	0.967	0.0327	2.604×10^{13}	18.414
$[CoL(H_2O)]Cl$ (formula weight = 475.5)	320	1:1	1.08	1.13	0.955	0.0442	6.333×10^6	9.335
		1:2	1.24	1.28	0.968	0.0312	2.604×10^{13}	18.414
	350	1:1	0.95	0.98	0.969	0.0306	1×10^7	9.608
		1:2	1.18	1.22	0.967	0.0327	2.604×10^{13}	18.414
$[Co(OH)L(H_2O)_2]$ (formula weight = 477)	255	1:1	2.44	2.47	0.987	0.0121	4.083×10^7	10.446
		1:2	2.66	2.69	0.988	0.0111	2.126×10^{14}	19.665
	305	1:1	1.40	1.44	0.972	0.0277	1.79×10^7	9.995
		1:2	1.54	1.58	0.974	0.0253	6.237×10^{13}	18.934
$[NiL(OH)]\cdot 2H_2O$ (formula weight = 477.5)	265	1:1	2.52	2.54	0.992	0.0078	16.5×10^7	11.279
		1:2	2.58	1.60	0.992	0.0076	17.18×10^{14}	20.911
	310	1:1	1.98	2.01	0.985	0.0149	4.083×10^7	10.446
		1:2	2.01	2.03	0.990	0.0098	2.126×10^{14}	19.665
$[CuL(OH)]\cdot 2H_2O$ (formula weight = 482)	265	1:1	1.52	1.54	0.987	0.0129	4.083×10^7	10.446
		1:2	1.56	1.58	0.987	0.0126	2.12×10^{14}	19.665
	310	1:1	1.98	2.01	0.985	0.0149	4.083×10^7	10.446
		1:2	1.84	1.86	0.989	0.0107	2.120×10^{14}	19.665
$[ZnL(OH)]\cdot 2H_2O$ (formula weight = 483)	305	1:1	1.78	1.82	0.978	0.0219	1.79×10^7	9.955
		1:2	1.90	1.93	0.984	0.0155	2.126×10^{14}	19.605
	350	1:1	0.86	0.90	0.955	0.0444	6.33×10^6	9.335
		1:2	1.20	1.24	0.967	0.0322	2.604×10^{13}	18.414

Table 2
Analytical and physical data of amoxicillin complexes

Compound	Colour (% yield)	mp (°C)	Found (calcd.) (%)				Found molecular ion [*m*/*z*] (calcd.)	μ_{eff} (BM)
			C	H	N	M		
$[FeL(OH)(H_2O)_2]$ ($C_{16}H_{24}FeN_3O_8S$)	Brown (70)	>300	40.05 (40.50)	5.00 (5.06)	8.68 (8.01)	10.90 (11.60)	475 (474)	5.24
$[Fe(OH)_2L(H_2O)]$ ($C_{16}H_{23}FeN_3O_8S$)	Brown (70)	>300	40.20 (40.50)	5.10 (5.06)	8.86 (8.40)	11.81 (12.00)	475 (473)	5.24
$[CoL(H_2O)]Cl$ ($C_{16}H_{21}ClCoN_3O_6S$)	Brown (60)	>300	40.25 (40.42)	4.42 (4.40)	8.80 (8.81)	12.00 (12.31)	473 (477)	2.24
$[Co(OH)L(H_2O)_2]$ ($C_{16}H_{24}CoN_3O_8S$)	Brown (75)	>300	40.42 (40.25)	5.03 (5.07)	8.80 (8.88)	11.94 (12.33)	478 (477)	2.5
$[NiL(OH)]\cdot 2H_2O$ ($C_{16}H_{24}NiN_3O_8S$)	Yellowish brown (66)	>300	40.17 (40.25)	5.03 (5.02)	8.41 (8.78)	12.26 (12.28)	478 (477)	Diamg.
$[CuL(OH)]\cdot 2H_2O$ ($C_{16}H_{24}CuN_3O_8S$)	Black (70)	>300	38.48 (38.48)	4.60 (4.60)	8.69 (8.42)	12.70 (12.71)	482 (484)	1.85
$[ZnL(OH)]\cdot 2H_2O$ ($C_{16}H_{24}N_3O_8SZn$)	Brown (65)	250	39.59 (39.97)	4.96 (4.97)	8.41 (8.87)	13.45 (13.48)	485 (483)	Diamg.

Diamag. = diamagnetic. The proposed general formulae of these complexes were found to be $ML(H_2O)_w(H_2O)_x(OH)_y(Cl)_z$, where M = Fe(II), Co(III), $w = 0$, $x = 2$, $y = 1$, $z = 0$; M = Co(II), $w = 0$, $x = 1$, $y = 0$, $z = 1$; M = Fe(III), $w = 0$, $x = 1$, $y = 2$, $z = 0$; M = Ni(II), Cu(II) and Zn(II), $w = 2$, $x = 0$, $y = 1$, $z = 0$, where also w = water of crystallization, x = coordinated water, y = coordinated OH^- and z = Cl^- in the outer sphere.

data obtained in the experimental part. The results obtained are shown in Table 1. It is clear from the data that, K_f for the Fe(II)–ACT system at λ = 325 nm, 1:1 (M:L) and 1:2 (M:L) complexes, range from 10^7 to 10^{13}; K_f of Fe(III)–ACT (1:1) is 10^7 at 255 nm; K_f for the Co(II)–ACT (1:2) at λ = 320 nm is 2.6×10^{13}; K_f for the Co(III)–ACT (1:2) at 255 nm is 2.1×10^{14}, etc. The high values of K_f ranging from 10^7 to 10^{14} for these complexes refer to their high stability in solution at pH values very close to that of in vivo system. The calculated values of ΔG range from 9.6 to 19.6 kcal mol deg^{-1} and confirm the stability. Therefore, the use of a higher dose of amoxicillin, than that recommended by the physician should be avoid. The elemental microanalyses for the separated, purified and analyzed solid complexes together with other analytical and physical data are given in Table 2. Thus, it is very interesting to prepare and to study such complexes in both solution and in the solid state to shed more light on the nature of bonding using IR spectra (Table 3) between 3d-block metal cations and the amoxicillin drug.

3.1. Infrared spectra of the solid complexes and mode of chelation

The infrared spectra of the solid complexes and the ACT ligand were recorded in the range 400–4000 cm^{-1}. The IR spectral data of ACT and its complexes and the assignment of the vibrational frequencies are given in Table 3. The highest frequency of the bands of the ligand at 3200 cm^{-1} can be assigned to the asymmetric ν(NH) vibration of the amino group. The other band at 3000 cm^{-1} may be due to the vibration of the imino group. These two bands are shifted on complexations indicating the involvement of both NH_2 and NH groups in complex formation. The shift of ν(NH) to lower frequency from 2968 to 2924–2927 cm^{-1} on complexation suggests coordination via the NH of the amide group. The absence of a C=O (β-lactame) ligand band at 1774 cm^{-1} and the appearance of the band at 1603–1523 cm^{-1} in all complexes, suggest that 6,7-enolization (Fig. 1) takes place before coordination with metal ions. The occurrence of bands at 625–520 cm^{-1} (M–N) and 420–455 cm^{-1} (M–O) prove the bonding of nitrogen and oxygen to the metal ions [11,12]. The spectra of the solid complexes exhibited a broad band at 3630–3440 cm^{-1}; which may be attributed to ν values of the water molecules of crystallization, while the band observed at 889–750 cm^{-1} may be assigned to coordinated water molecules in the complexes.

3.2. Electronic spectra and magnetic susceptibility

The room temperature magnetic moment value of 5.7 BM of the Fe(III) complex is within the range corresponding to the high-spin octahedral Fe(III) complexes. For the Fe(II)–ACT complex, the obtained magnetic moment of 5.33 BM indicates octahedral geometry of ligands around the metal cation. The μ_{eff} value of the Co(II)–ACT complex is found to be 2.24 BM, consistent with square–planar geometry [12]. This

Table 3
Selected IR data (4000–200 cm^{-1}) for amoxicillin and its complexes

Compound	ν(C–N) (cyclic)	$\nu(NH_2)$	ν(C=O) (β-lactame)	ν(NH) (amide)	ν_{asym-} (COO^-)	ν(M–O) (β-lactame)	Coordinate H_2O	ν(M–N)
Amoxicillin	1379 s	3200–3000 s	1774 s	2968 s	1582 s	–	–	–
$[FeL(OH)(H_2O)_2]$	1376 s	3251 b	disap.	2925 s	1603 s	426 s	888, 796 s	615 s
$[FeL(OH)_2(H_2O)]$	1379 s	3157 b	disap.	2924 s	1601 s	455 s	889, 795 s	540 s
$[CoL(H_2O)]Cl$	1373 s	3276 b	disap.	2927 s	1602 s	430 s	840, 750 s	586 s
$[Co(OH)L(H_2O)_2]$	1380 s	3229 b	disap.	2926 s	1602 s	420 s	841, 750 s	535 s
$[NiL(OH)]\cdot 2H_2O$	1377 s	3278 b	disap.	2926 s	1601 s	430 s	841, 750 s	519 s
$[CuL(OH)]\cdot 2H_2O$	1384 s	3251 b	disap.	2924 s	1599 s	447 s	841, 775 s	625 s
$[ZnL(OH)]2H_2O$	1390 s	3258 b	disap.	2925 s	1601 s	420 s	842, 780 s	599 s

s = strong, b = broad and disap. = disappeared peak.

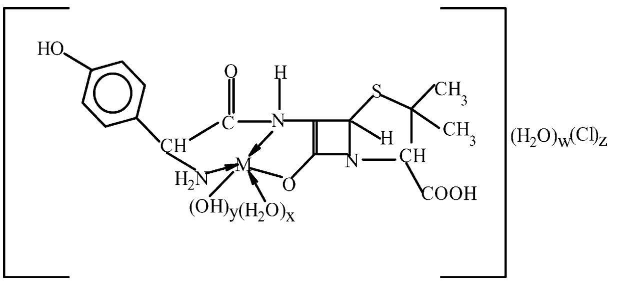

Fig. 2. The proposed structural formulae of amoxicillin–d-block complexes, where M = Fe(II), Co(III), $w = 0$, $x = 2$, $y = 1$, $z = 0$; M = Co(II), $w = 0$, $x = 1$, $y = 2$, $z = 1$; M = Fe(III), $w = 0$, $x = 1$, $y = 2$, $z = 0$; M = Ni(II), Cu(II) and Zn(II), $w = 2$, $x = 0$, $y = 1$, $z = 0$, where also w = water of crystallization, x = coordinated water, y = coordinated OH^- and $z = Cl^-$ in outer sphere.

result may be due to the reduction of Co(III) to Co(II) during complexation by the thiazol sulfur atom. The spectrum of these complexes reveal bands at 424 and 416 mm suggesting the presence of square–planar geometry around cobalt ions. The room temperature magnetic susceptibility data of the Ni(II)–ACT complex shows that, the complex is essentially diamagnetic and of low-spin with ${}^1A_{1g} \rightarrow {}^1A_{2g} \rightarrow {}^1E_g$ transitions, respectively [12]. The complex is, therefore, of square–planar geometry because it is a diamagnetic and there is no band seen below 1000 nm.

The observed $\mu_{\text{eff}} = 1.85$ BM of the Cu(II)–ACT complex is very close to the spin-only value [11] of an unpaired electron (1.73 BM) which indicates that the orbital contribution is almost quenched by the crystalline field. Electronic spectra of

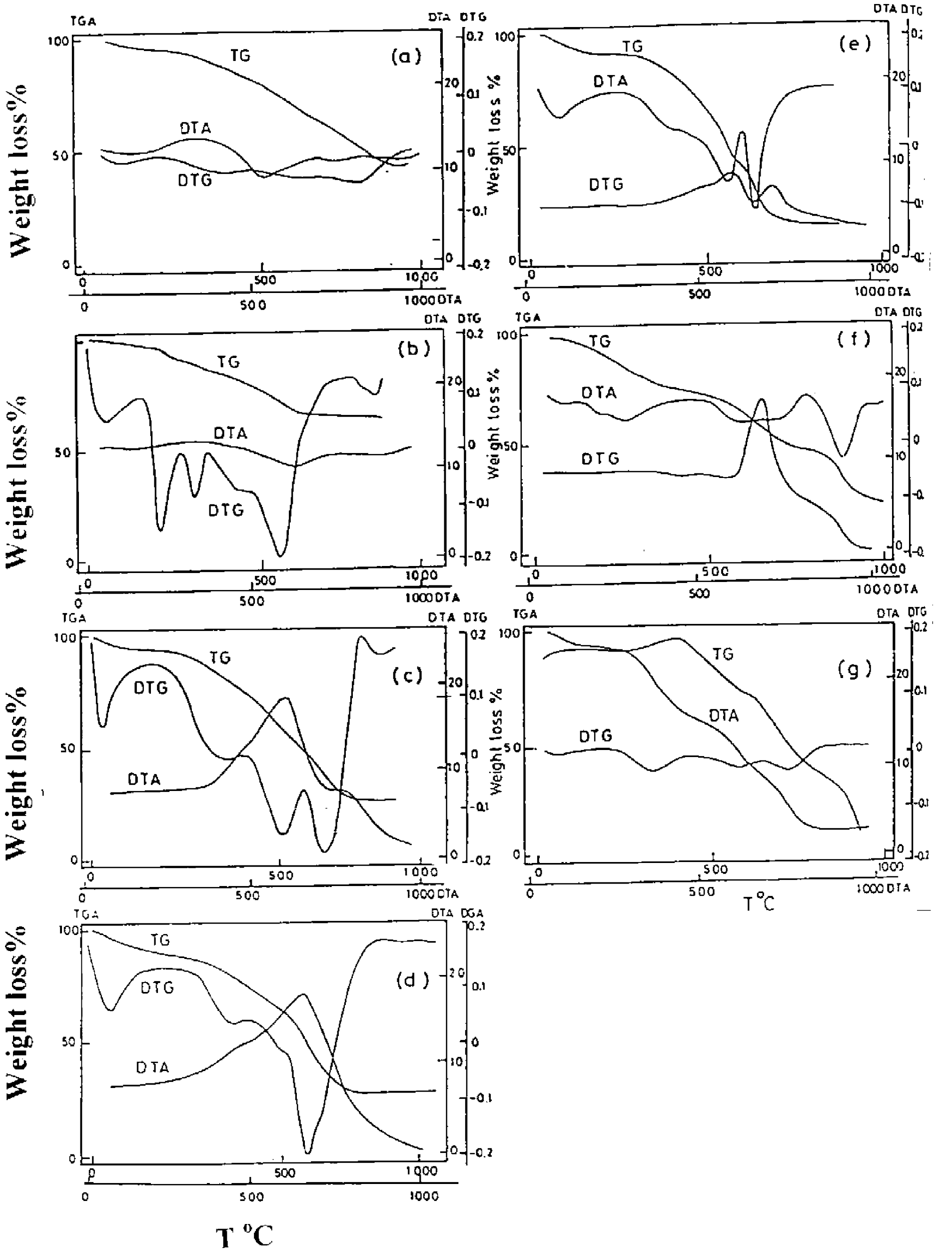

Fig. 3. Thermal analyses (TGA, Dr.TGA and DTA) of amoxicillin trihydrate (ACT) complexes of 3d-transition metals.

the complex show only three bands in the region 550–460 nm due to the transitions $^2B_{1g} \rightarrow {}^1A_{1g} \rightarrow {}^1E_g$ and charge transfer, respectively [12], which corresponds to square–planar geometry [12]. The Zn(II)–ACT complex is diamagnetic and has a tetrahedral structure as confirmed by its electronic transition spectra.

The structural formulae for all of the proposed complexes of d-block element–ACT are illustrated in different shapes varied between the square–planar and octahedral forms given by Fig. 2.

3.3. Thermal analyses and mass spectra of the solid complexes M–ACT

3.3.1. Thermal analysis and mass spectra of the Fe(II)–ACT complex

The thermal analyses of theses complexes are shown in Fig. 3 and their mass spectra are shown in Fig. 4. Fig. 3 shows the TG and DTA data of all studied complexes. The detailed description and explanation of TA data of the prepared and studied M–ACT complexes are given in Table 4. These data reasonably account for the loss of water molecules [12] and parts of the decomposed ligand during the heating processes [13]. The Fe(II)–ACT complex is thermally decomposed at several stages (Table 4) and the total weight loss is 55%, leaving as residue a stable oxide $Fe\cdot F_2O_3$ [12] of mole mass 214 and 45%. The DTA confirms the thermal decomposition of this complex. There is an exothermic broad peak at 200–456 °C; which may be attributed to the loss of some ACT ligand parts that chemically recombined. This exothermic process required energy of 1.31 J g^{-1} at 27–380 °C and its maximum occurs at 315 °C. The complete process required 383 J g^{-1} of energy.

The mass spectra of the Fe(II)–ACT complex of the mole mass 475 show a molecular ion at $m/z = 475$ (RI = 4.72%). This is followed by a molecular ion of $m/z = 214$ (RI = 25%) of the residual oxide of mole mass 214 [12].

3.3.2. Thermal analysis and mass spectra of the Fe(III)–ACT complex

The thermal decomposition process of the Fe(III)–ACT complex occurs in five stages (Table 4) as a result of the decomposition of ACT ligand together with the loss of water molecules, total weight loss 36%, leaving $Fe_3O_4\cdot FeO$ as 64% of a stable residue of mole mass 304. The DTA of this complex shows a broad exothermic peak at a temperature range 219–470 °C; which may be attributed to the exothermic decomposition of this complex and chemical recombination of the fragments of the ligand obtained. This process required an energy of 2.11 kJ g^{-1}.

The mass spectra of the Fe(III)–ACT complex show a molecular ion of $m/z = 474$ (RI = 4.3%) of the main complex (calcd. MW: 474), together with a residual oxide (calcd. MW: 304) appeared as a molecular ion of $m/z = 304$ (RI = 25.8%).

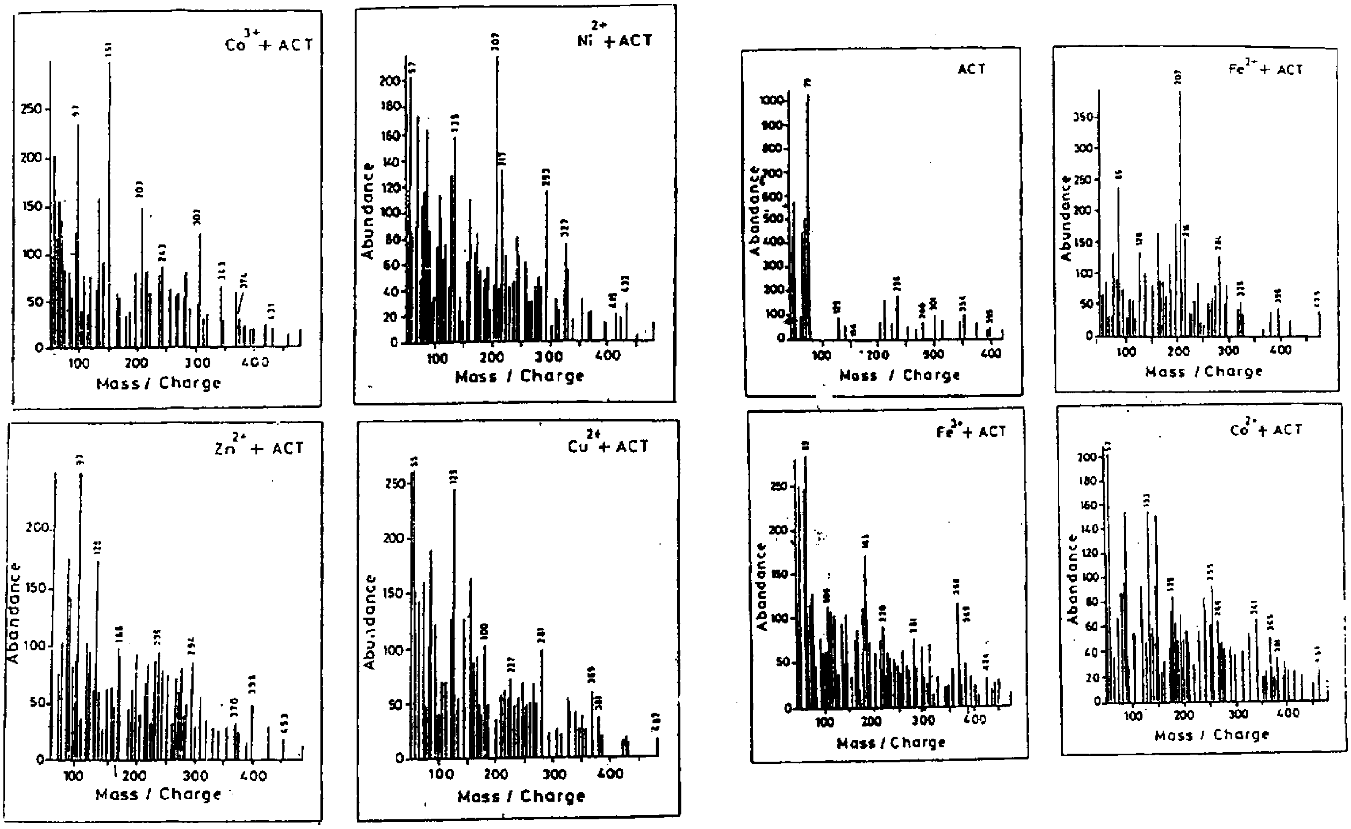

Fig. 4. Mass spectra of ACT–d-block elements complexes.

Table 4
Thermal decomposition data of amoxicillin (ACT) complexes

Complex	Temperature range in TG (°C)	Peak temperature in TG (°C)	Mass loss (%)		Assignment
			Calcd.	Found	
$[FeL(OH)(H_2O)_2]$	23–140	68.58	3.79	3.45	Loss of H_2O molecule (water of hydration)
	143–306	241.24	17.9	17.64	Loss of CONH and $CH_3C{-}CH_3$ molecules
	306–412	366.15	15.6	16.68	Loss of C_2S and H_2O molecules (coordinated)
	425–565	471.47	17.08	17.69	Loss of $HC{\equiv}C{-}CN$, CHNH, C_6H_4OH, and Fe_3O_3 (45%)
$[Fe(OH)_2L(H_2O)]$	20–137	72.35	3.37	3.25	Loss of CH_4 molecule
	138–220	181.86	6.75	6.17	Loss of CH_3OH molecule
	220–280	248.44	3.8	4.8	Loss of H_2O molecule (coordinated)
	283–262	323.89	5.9	6.84	Loss of a CO molecule
	363–569	424.52	15.4	14.69	Loss of $NCH_2CH_2O$and leaving $Fe_3O_4{\cdot}FeO$ (64%) as residue
$[CoL(H_2O)]Cl$	31–170	70.89	6.31	7.43	Loss of C_2H_6 molecule
	170–360	297.26	19.55	19.37	Loss of C_6H_4OH molecule
	360–485	428.95	25.47	24.56	Loss of CO_2, 1/2 Cl and CH_2CH_2N molecule
	485–610	529.48	23.55	23.85	Loss of C_2S and H2NCH2(NH)CH and of Co_2O_3 (26%) as a residue
$[Co(OH)L(H_2O)_2]$	20–125	62.62	10.06	9.47	Loss of C_2H_6 and H_2O molecules (coordinated)
	128–301	248.01	17.8	17.52	Loss of CO_2 and C_2H_2NH molecules
	303–513	389.95	46.73	45.71	Loss of C_6H_4OH, $H_2NCHCONH$ and Co_2O_4 (38%) as a residue
$[NiL(OH)]{\cdot}2H_2O$	20–170	172.91	10.06	9.59	Loss of C_2H_6 and H_2O molecules (water of crystallization)
	170–440	357.15	50.31	51.75	Loss of CH_2COOH + H_2N + $N_2NCHCONH$ and C_6H_4OH molecules
	440–600	458.53	23.29	24.8	Loss of CO + C_3S, H_2O and NiO (15%) as a residue
$[CuL(OH)]{\cdot}2H_2O$	24–128	83.13	3.6	3.33	Loss of H_2O molecule (crystallization)
	131–450	262.67	21.8	21.86	Loss of CO_2 and C_2H_6 molecules
	451–780	624.11	27	26.11	Loss of C_6H_4OH and $CH_2{=}CH_2N$ molecules
	790–996	882.28	22.4	23.26	Loss of L parts and CuO_3 (24%)as a residue
$[ZnL(OH)]{\cdot}2H_2O$	31–158	70.22	6.21	5.95	Loss of C_2H_6 molecule
	160–406	289.21	34.78	34.51	Loss of C_6H_4OH, H_2O (of crystallization) and H_2NCHO molecules
	409–525	471.87	22.53	22.03	Loss of H_2O (of crystallization), CO_2, and CH_2CHNH molecules
	529–718	581.27	20.91	23.46	Loss of $HO{-}CH_2CH_2NCS$ and leaving ZnO (17%) as a residue

3.3.3. Thermal analysis and mass spectra of the Co(II)–ACT complex

The Co(II)–ACT complex thermally decomposed in several stages (Table 4) of a total weight loss of 74%, leaving a stable Co_2O_3 of mole mass 127 and 26%. The mass spectra of Co(II)–ACT (calcd. MW: 475.5) show a molecular ion of m/z = 477 (RI = 5.91%) referring to the main complex, followed by a molecular ion of m/z = 126 (RI = 13%) of the stable final residue of Co_2O_3 (calcd. MW: 127). The gradual appearance of molecular ions in mass spectra supports the gradual mass losses given by TA.

3.3.4. Thermal analysis and mass spectra of the Co(III)–ACT complex

The TG of Co(III)–ACT complex, refers the total mass loss of 62% due to the fragmentation of the complex in four stages (Table 4), leaving Co_2O_4 as a sable residue (calcd. MW: 184 and 38%). All of the above mass losses appear in DTA of this complexes as a broad exothermic peak in the temperature range 20–448 °C and these stages required energy values of −83.5, −278.0, −103.6 $cal\,g^{-1}$ and 389.8 $J\,g^{-1}$, respectively.

The mass spectra of the main complex (calcd. MW: 477) give a molecular ion of m/z = 478 (RI = 6.06%) followed by molecular ions, of m/z = 93 of phenol ion (calcd. MW: 94 and 41.4%) and final molecular ion of m/z = 183 (RI = 13%) of the residual oxide [12].

3.3.5. Thermal analysis and mass spectra of the Ni(II)–ACT complex

The TG of Ni(II)–ACT complex exhibits total mass losses of 84% leaving a stable NiO (calcd. MW: 75.5 and 16%).

The mass spectra show a molecular ion of m/z = 478 (RI = 5.96%) referring to the main complex Ni(II)–ACT, together with a final residue of NiO (calcd. MW: 75.5) appeared as a molecular ion of m/z = 75 (RI = 18.81%).

3.3.6. Thermal analysis and mass spectra of the Cu(II)–ACT complex

The Cu(II)–ACT complex thermally decomposed in several stages (Table 4) of the total mass loss of 76% leaving a stable $CuO{\cdot}2H_2O$ as a residue of mole mass 115.5 and remain percent 24%.

These mass losses appear in DTA as endothermic peaks centered at 630 and 693 °C. The Cu(II)–ACT complex (mole mass = 482) appears in mass spectra a molecular ion of m/z = 481 (RI = 5.77%) together with another molecular ion of m/z = 370.5 (RI = 10.77%) leaving a residue of CuO_3 (calcd. MW: 114.5) appears as molecular ion of m/z = 114 (RI = 93.08%).

3.3.7. Thermal analysis and mass spectra of the Zn(II)–ACT complex

The TG of Zn(II)–ACT complex thermally decomposed in several stages of total loss 84% leaving a stable ZnO of mole mass 81 and remain percent 16% as a stable residue. In mass spectra of Zn(II)–ACT complex (calcd. MW: 483) it appears as a molecular ion of $m/z = 484$ (RI = 4.44%) followed by the molecular ion of $m/z = 453$ (6.85%), a molecular ion of $m/z = 284$ (RI = 19.76%), a molecular ion of $m/z = 182$ (RI = 19.16%) and finally a residual molecular ions of $m/z = 81$ (RI = 7.66%) referring to ZnO (calcd. MW: 81).

The detailed description of TA behavior of different M–ACT complexes in comparison with their mass spectral behavior; leads to the conclusion that most of the molecular ions appeared in mass pathways are those obtained as a result of stepwise thermal degradation of these complexes. This means that generally mass spectral passways are correlated to the obtained pathways in thermal analyses (TA) [13,14]. The main difference is that TA detect remaining part of the complex but mass detect most and/or the fragments as molecular ions. Therefore, both mass and TG support each other and act as complementary tools as previously concluded by several research papers done in this laboratory [12–16]. The TA and mass spectra of these complexes, in comparison with, IR, magnetic and the reflectance spectral analyses of these complexes, elucidated the proposed structures of these complexes.

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