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Recent advances in the structure elucidation of d^{10} transition metal complexes based on 16-membered ring macrolide drug

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The present study outlines theoretical and spectroscopic investigations on a Tylan® ligand and some of its d^{10} transition metals complexes. Tylan interacts in a bidentate coordination manner through donor atoms of oxygen and nitrogen in its structure. Two essential Tylan metal complexes have been synthesized and characterized depending on their elemental analysis, molar conductivity and spectral studies (FT-IR and Mass spectra). The very low value of molar conductivity of complexes demonstrates their non-electrolytic nature. From experimental studies, general structures of these new complexes have been assumed as formula $[M(TYS)X_2(H_2O)_2]$, where TYS = Tylan ligand; M = Hg(II) and Cd(II); X = Cl^-. Based on spectroscopic studies, an octahedral geometry has been suggested for both complexes. Molecular modelling by Gaussian 09 software has been employed to give further light on bonding properties in addition to theoretically confirming binding sites of Tylan ligand and its new synthesized metal complexes. The quantum chemical reactivity parameters such as chemical hardness, chemical potential, electronegativity, electrophilicity index and HOMO-LUMO energy gap have been obtained theoretically. The thermal analysis by TG-DTA indicates that the complex has three consecutive phases of decomposition which ends by the formation of divalent metal oxide, CdO as a final product. While in case of Hg complex no metal oxide formation is observed due to Hg(II) sublimation. The kinetic and thermodynamic parameters have been calculated utilizing DTA curves. This study explains that Tylan ligand can form five-membered ring with metal ion Cd(II) and Hg(II) during formation of complexes which gives high stability to the synthesized complexes.

Keywords: Macrocyclic, Mass Spectra, Molecular Modelling, Mercury Complexes, Thermal Studies

Tylan® is a soluble powder veterinary drug. It is a trade name for the 16-membered ring macrolide antibiotic tylosin. It is also known as tylosin A which is the most abundant compound of its formulation as reported[1,2]. Tylosin A is highly hygroscopic substance, chemical formula is $C_{46}H_{77}NO_{17}$, and molecular weight is 916.112 gm /mol, meting point range in between “128°C - 132°C” and its chemical structure shown in Fig. 1. It is white to buff colour with high degree of solubility in water by 5 mg/ml at 25°C. Its solutions are stable between *p*H4 and *p*H9, while at *p*H<4 another active compound, desmycosin, is formed[3].

Tylosin A is considered as broad-spectrum antibiotic and shows strong activity against Gram-stained bacteria Positive: Staphylococcus, Streptococcus, Coryne, Clostridium, and secondary bacteria associated with viral diseases. There are some types of Gram-negative bacteria; Pasteurella and Campylobacter that are also affected by the effect of tylosin. From literature it is crucial for the treatment of infectious illnesses like mastitis and asthma also. It is mostly utilized as a feed supplement to encourage the growth of young animals[4-7]. Tylosin mechanism of action summed by binding to 23S rRNA of the bacterial ribosomal 50S subunit, which inhibits destructive bacterial effect[8].

The lack of adequate studies highlighting the importance of the coordination of macrolides towards transition metal ions, particularly the capacity of 16-membered macrolide antibiotics to bind d-block series

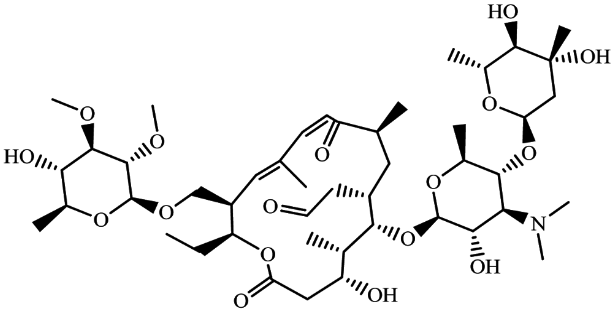


Fig. 1 — Chemical structure of Tylosin A

elements was the motivation to our previous work[9] which discussed complexation of tylosin with different metal ions such as Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II). Also, we decided to continue researching in the coordination of tylosin which is chosen as target suitable for macrolide ligand towards Hg(II) and Cd(II) metal ions. The primary objective of this research was to focus on the synthesis, characterization, spectral, thermal study and molecular modeling studies of some recent Tylan or tylosin A (TYS) metal complexes.

Experimental Section

Materials

This starting ingredients in our work Tylan® and metal chlorides were all purchased from VAPCO and Piochem companies. Transition metal chloride salts and ligand are of high purity; mercuric chloride AR $HgCl_2$ (99.5%), Cadmium Chloride, anhydrous $CdCl_2$ (98%). All chemicals were used without any further purification in our laboratory while Tylan® (containing > 90% tylosin A) was dried at 105°C before using directly due to its highly hygroscopic ability.

Synthesis of Tylan metal complexes

Tylan ligand was dissolved in distilled water, while metal chlorides of Hg(II) and Cd(II) were dissolved in ethanol 70%. Several molar ratios were further studied until the stoichiometry of (M:L) was reached. 40 ml of dissolved heated ethanol solution of chlorides and inorganic salts of transition metal ions are mixed with water soluble ligand. The reaction mixture was refluxed for around 30 minutes. After 12 hours, the high yield precipitated complexes were determined to identify the molar ratio of the predicted amount of ligand and the molar amount of the metal chloride salt interacted. After filtering, washing multiple times with a 50% ethanol solution, and letting to dry on open air all day, the synthesized complexes were finally prepared for analysis.

Methods and Instruments

Elemental Analysis and metal ion content (%) determination

Carbon, hydrogen and nitrogen analysis of Tylan and both complexes measured, at central lab, Cairo University and the contents of all the synthesized complexes were analysed by the normal method.

The metal ions contents were determined by using model AA-6650 Shimadzu atomic absorption spectrophotometer instrument. Solutions for determining the metal concentrations were prepared by digesting 0.040 g of each metal complex with 5 ml of conc. HCl and conc. HNO_3 in the ratio (3:1). The volume was then diluted to 100 ml with distilled water in 100 ml calibrated flasks. After that, the amount of metals was quantified against the blank solution[10]. The result of metal ions ratio was confirmed by complexometric titration against EDTA[11].

Physical Measurements

The well-known Volhard method[12] was used in an acidic medium to analyse the complexes chloride contents. Melting points were measured by using FALC melting point device model 2013.

Molar conductivity of complexes with 10^{-3} M in DMSO was done by using AD410 Adwa conductivity meter and measured by dissolving both metal complexes in DMSO at 25°C ± 2°C by concentration 1×10^{-3} M, and samples were measured by recommended procedure[13].

The Fourier-transform infrared spectra

FT-IR spectra of Tylan and both synthesized metal complexes were obtained in a KBr disc using The Bruker Tensor 37 FT-IR instrument which is located in the central lab, Alexandria university, covering frequency range of 400 - 4000 cm^{-1} and the data recorded and refined by OPUS Data Collection Program.

Fast atom bombardment (FAB) mass spectrum

FAB mass spectrum of the Tylan ligand and its Cd(II) complex were recorded on a Shimadzu Qp-2010 Plus spectrometer at the Regional Centre for Mycology and Biotechnology, Al-Azhar University, Cairo, Egypt.

Thermal Analysis

Differential thermal analysis (DTA) and thermo gravimetric analysis (TG) of Tylan ligand and its metal complexes were carried out using the instrument LINSEIS PT1600 which is located in the central lab-faculty of science, Alexandria university. The rate of heating was 10°K/min. The cell used was platinum and the atmospheric nitrogen rate flow was 15 ml/min.

Computational calculations

The ligand was optimized using the DFT approach with the B3LYP/6-311+G(d,p) level of theory using the Gaussian 09 program[14].

Result and Discussion

Elemental Analysis and Physical Properties

The physical characteristics of the free ligand and both metal chelates, as well as the findings of elemental analyses, are reported in Table 1 and are in good conformity with the proposed formulae. The isolated solid complexes are entirely soluble in polar aprotic solvents like DMF and DMSO, while they are only partially soluble in polar organic solvents at room temperature. It can suggest the general structural formulae of 1:1 (M:L) complexes based on the aforementioned results.

Molar Conductivity Measurements

The obtained molar conductance results are collected in Table 1. The molar conductivity value of Hg(II) and Cd(II) chelates of free ligands were found to be 5.65 and 9.32 $\Omega^{-1}\cdot cm^2\cdot mol^{-1}$, respectively. The chelates are non-ionic in nature and they are considered as non-electrolytes which conform the formulae $[M(TYS)X_2(H_2O)_2]$ for the new complexes[15].

Fourier transform infrared spectroscopy (FT-IR) of Tylan and its metal complexes

The FTIR spectra of ligand Tylosin A was discussed and illustrated well on literature[9,16]. Moreover, in this paper only significant bands were considered and explained, Table 2 and Fig. 2 provide the spectra data of ligand and it's both metal complexes. The peaks at 3450 cm^{-1} were attributed to the O–H stretching vibration of hydroxyl groups or H_2O molecules and the absorption bands in the range of (2830-2840) cm^{-1} are assigned to the C–H group. Peaks in the range (1720-1725) cm^{-1} were also observed in the spectral sheets of tylosin A ligand and its metal complexes, which belong to the lactone carbonyl group (C=O axial strain). This is strong evidence for the lack of coordination occurrence between the lactone carbonyl group and the metal ions. The C–N group appears in the absorption band at 1250 cm^{-1}while has been red shifted to 1132 and 1207 cm^{-1} for Hg(II) and Cd(II) complexes, respectively which explains that those metal ions maybe coordinated with 3° amine group to form new

Table 1 — Elemental analysis, molecular formula, stoichiometry's, yield, Melting point, colour and Molar Conductivity of Tylan metal complexes

Compd		$[Hg(TYS)Cl_2(H_2O)_2]\cdot 2H_2O$	$[Cd(TYS)Cl_2(H_2O)_2]\cdot 2.5H_2O$
		1:1	1:1
Empirical Formula		$C_{46}H_{85}Cl_2HgNO_{21}$	$C_{46}H_{86}Cl_2CdNO_{21.5}$
Formula Weight (gm/mol)		1258.98	1179.80
Colour		Off-white	Yellowish white
Elemental Analysis, calculated (Found)%	C	43.88 (43.18)	46.83 (46.04)
	H	6.75 (6.90)	7.28 (7.15)
	N	1.11 (1.25)	1.19 (1.22)
	M	15.93 (15.60)	9.53 (9.70)
	Cl	5.63 (5.45)	6.01 (5.72)
Yield (%)		84%	89%
Melting point (°C)		310 - 313	342 - 344
Molar Conductivity ($\Omega^{-1}\cdot cm^2\cdot mol^{-1}$)		5.65	9.32

Table 2 — Assigned vibrational FTIR bands spectra of Tylan ligand and its metal complexes.

Compd	$\nu_{(C=O)}$lactone	$\nu_{(OH)}$	$\nu_{(C-O)}$	$\nu_{(C-N)}$	$\nu_{(C-H)}$	$\nu_{(M-N)}$	$\nu_{(M-O)}$
Tylan® (Tylosin A)	1720	3450	1120	1250	2840	—	—
$[Hg(TYS)Cl_2(H_2O)_2]\cdot 2H_2O$	1720	3440	1115	1132	2830	590	485
$[Cd(TYS)Cl_2(H_2O)_2]\cdot 2.5H_2O$	1725	3450	1050	1207	2830	582	477

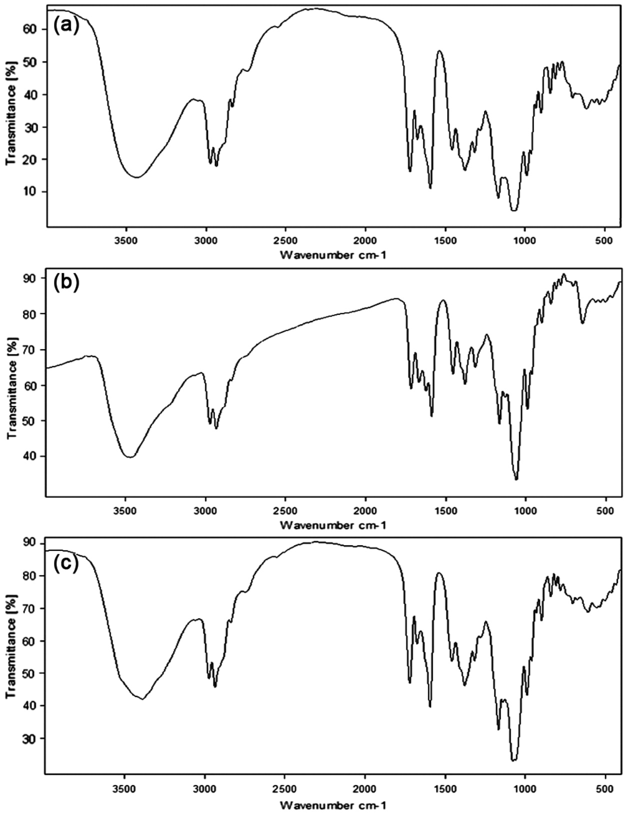


Fig. 2 — FT-IR spectra of ligand and its metal complexes, while **(A)** TYS ligand, **(B)** Hg-TYS complex and **(C)** Cd-TYS complex.

metal complexes. In addition, the noticed stretching vibration of M–Nat590 and 582 cm^{-1} which are absent in the spectra of ligand provides evidence of coordination bond between the metal ion through amine group.

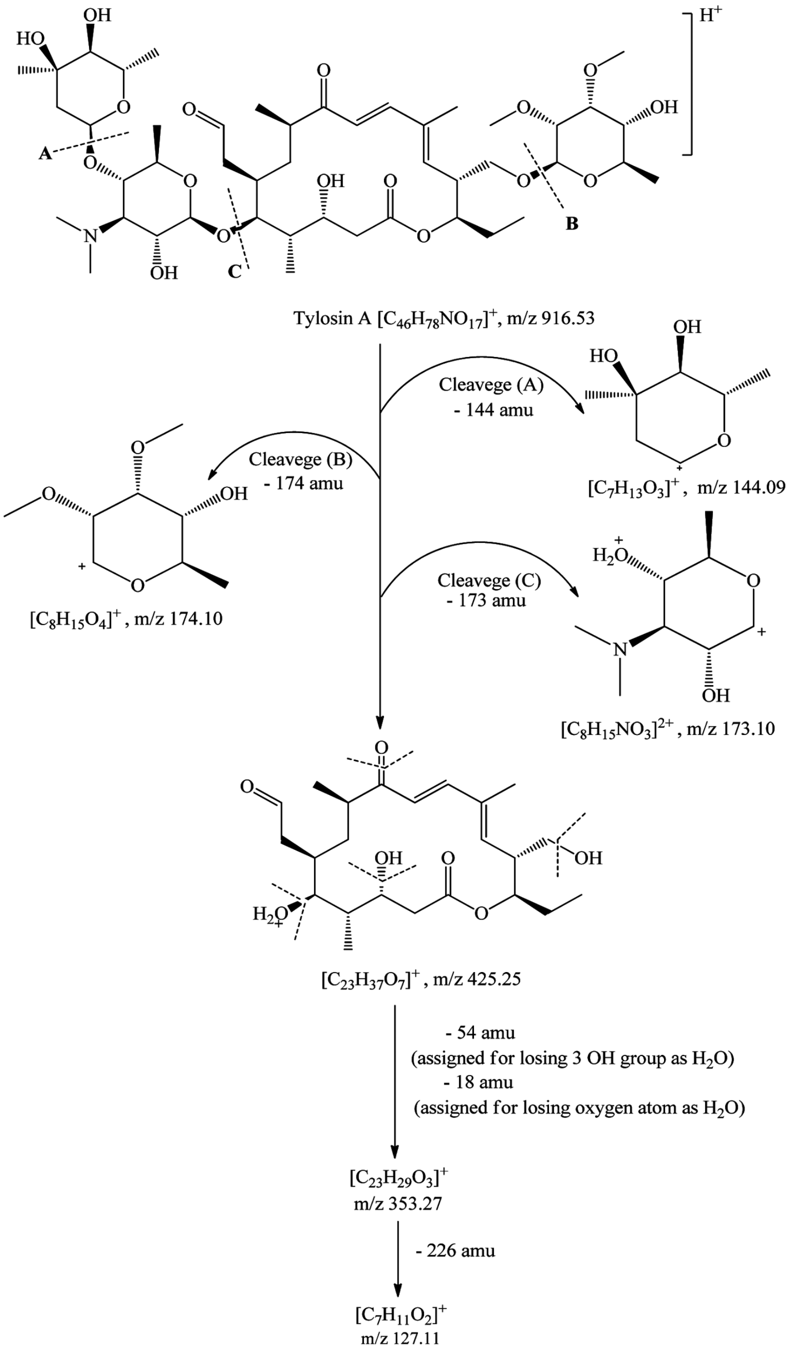
Mass spectrum of Tylan and Cd(II) complex

Mass spectrometry is an effective technique for estimating molecular weight and elucidating structure of metal complexes. Moreover, it provides data about the mechanism of fragmentation[17]. The mass spectrum investigation of the ligand Tylan (tylosin A) revealed an identical parent molecular ion peak components $[M+H]^+$ at m/z 916.526amu, which was consistent with the molecular weight predicted. The fragmentation suggested that the mechanism of tylosin A (Scheme 1) begins by the breakage of the glycosidic bond between the mycaminose and mycarose at the latter's side leading to a loss of 144 amu. The product ion for tylosin A at m/z 772 amu lacks the mycarose sugar. The yield of product ions at m/z 598amu that noticed in mass spectral sheet, shown in Fig. 3, is due to breaking of glycosidic bond between mycinose and the tylonolide ring at the sugar's side, causing the product ion of tylosin to lose the 174 amu which pointed to lose of mycinose sugar. The product ion at m/z 598 amu, further lost the mycaminose sugar which is 173 amu that lost as a result of the cleavage of glycosidic bond between the mycaminose sugar and the C_5 hydroxyl group of the tylonolide ring that lead to the formation of aglycones with m/z 425amu. It is worth noting that the presence of an observed ion at m/z 318amu, corresponding to reformation of the disaccharide mycarose and mycaminose[18,19]. After that, it was proposed that the aglycones of tylosin A lost four water molecules (72 amu) sequentially which is proven by the presence of peak at m/z 355amu. The fragments, their molecular weight and relative intensity (%) are presented in Table 3. In mass spectrum Fig. 4, the peak recorded at m/z = 1135 amu which referred to the mass of $[Cd(TYS)Cl_2(H_2O)_2]$ complex and elucidated 1:1 (M:L) structure.

As earlier studies[20,21] indicated the Hg(II) and Cd(II) have d^{10} configuration and no electronic spectra is produced. Hence, the geometry of both complexes was proposed as octahedral or distorted octahedral depending on the bidentate nature of Tylan ligand. Also the presence of two chloride ions and two water molecules in the inner sphere of complex that deduced from different spectroscopic tools used in this study, proves that the metal ion has six coordination number. From the above we conclude that the structures of both complexes are as shown in Fig. 5.

Thermal Analysis Studies

Thermogravimetric (TG) studies are an extremely helpful technique for monitoring the thermal degradation of solid materials that involve both simple metal salts along with complexed compounds[22]. The thermal cracking curve for the complex $[Hg(TYS)Cl_2(H_2O)_2].2H_2O$ (Fig. 6), showed three successive peaks where all of them were exothermic except the first one. These peaks spotlighted with the T_{max} near to the values 94.2, 330.2 and 402.8°C, respectively. The energies of activation and orders of decomposition reaction for these steps are (12.990 KJ/mol, 1.36), (29.039 KJ/mol, 1.11) and (115.89 KJ/mol, 1.9), respectively. The TG data sheet is accompanied by major distinctly three phases of cracking with different mechanism for each phase. The first temperature extent that appeared at (35.3-186.8)°C with ratio of mass decrease equal to 2.8% that



Scheme 1 — Suggested fragmentations steps for Tylan (tylosin A) ligand.

assumed to removal of nearly 2 moles of outer sphere water.

The second specified temperature range (186.8-425.0)°C distinguished with mass loss 66.94% assigned to exit of two moles of coordinated water and the other compound as assumed in the designated Scheme 2. The last specified temperature range for Hg(II) complex (425.0-695.9)°C with ratio of mass decrease equal to 27.30% that assigned to eliminate one mole of HgO and the rest of bulky complex except the ratio about 2.98% which represented the residue percentage for this complex and assumed to remain for three molecules of non-decomposed carbon[23].

The values of activation thermodynamic parameters, such as activation energy (ΔE*), enthalpy

Table 3 — Mass spectrum fragmentations of Tylan (tylosin A) ligand

Assignment	Molecular weight	m/z	Relative intensity (%)
$[M+H]^+$	916.112	916.526	45
$[C_{39}H_{66}NO_{14}]^+$	772.41	772.4478	8
$[C_{31}H_{52}NO_{10}]^{++}$	598.3284	598.3594	81
$[C_{23}H_{37}O_7]^+$	425.2391	425.2534	9
$[C_{23}H_{35}O_6]^+$	407.2401	407.2428	24
$[C_{23}H_{33}O_5]^{++}$	389.2411	389.2323	11
$[C_{23}H_{29}O_3]^+$	353.2431	353.2787	43
$[C_7H_{11}O_2]^+$	127.0729	127.1176	11

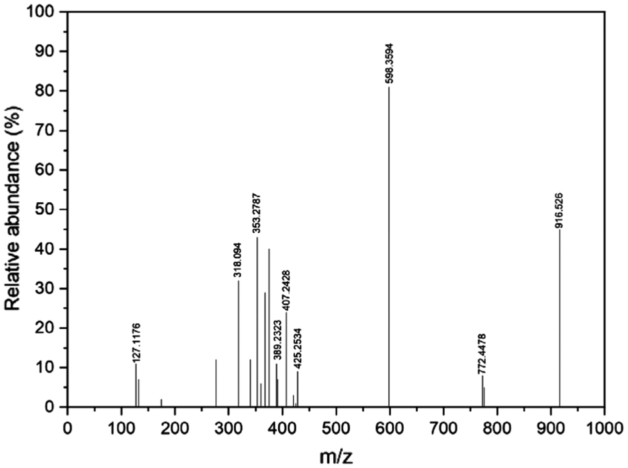


Fig. 3 — Mass spectrum for Tylan (tylosin A) ligand.

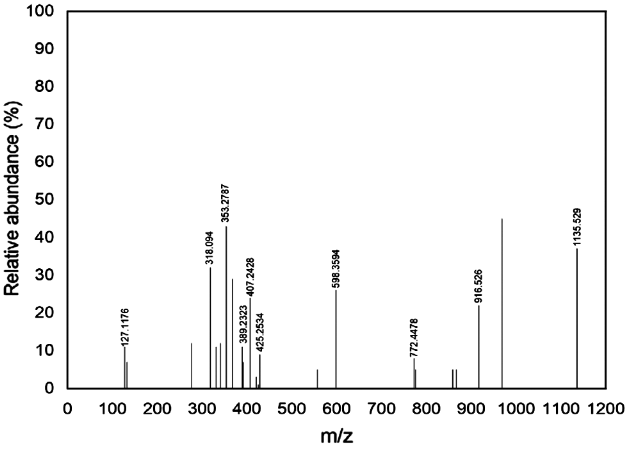


Fig. 4 — Mass spectrum of $[Cd(TYS)Cl_2(H_2O)_2]$ complex

of activation (ΔH*), entropy of activation (ΔS*) and order of reaction have been calculated as shown in the Fig. 7, which showed the direct relation between lnΔT and $10^3/T$ that give the value of slope for three steps as following –1.56248 peak 1, –3.4929 peak 2 and –13.9398 peak 3 and from calculations,[24] the values of thermodynamic parameters were calculated and summarized in the Table 4.

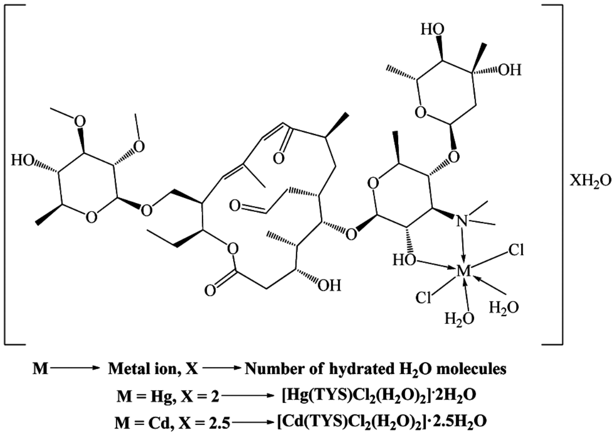


Fig. 5 — Proposed structure of M(II)-TYS complexes, Where M = Hg(II) or Cd(II).

Molecular Modeling for Tylan (tylosin A) Ligand

Molecular modeling is a collective term that refers to theoretical methods and computational techniques to model the behavior of molecules. The molecular modeling calculations are widely increasing nowadays for the expectation of the mechanism of the reactions and the identification of the products, this saves time and money. Thus, the synthesis and structures of new complexes are significant for understanding the complexation of metal ions with ligand and predicting the most stable structure of ligand and its metal complexes. Additionally, coordinated sites of metal ions with the free ligand may be formed, providing theoretical confirmation for the experimental results regarding the donor atoms[25,26].

From molecular modeling data including charges, bond lengths, bond angles and dihedral angles (Table 5), it is noted that tylosin A can coordinate to different metal ions through oxygen O(45) of OH group of mycaminose sugar and N(42) of 3° amine group as shown in Fig. 8, which has the charge values for O(45) and N(42) as –0.391725 and –0.128883, respectively. Oxygen and nitrogen atoms of these

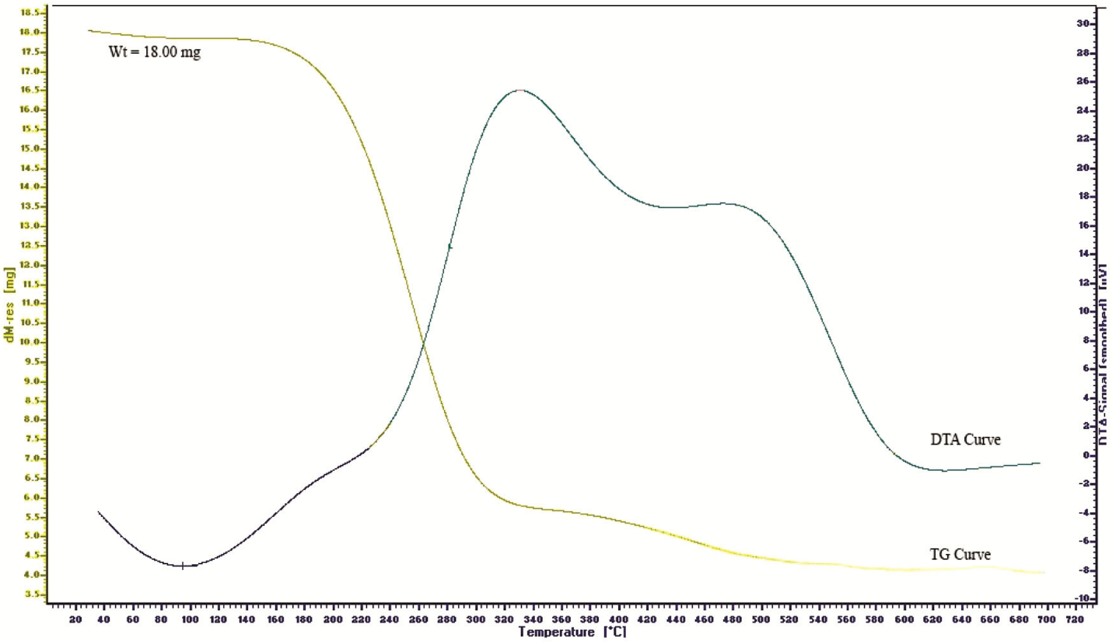
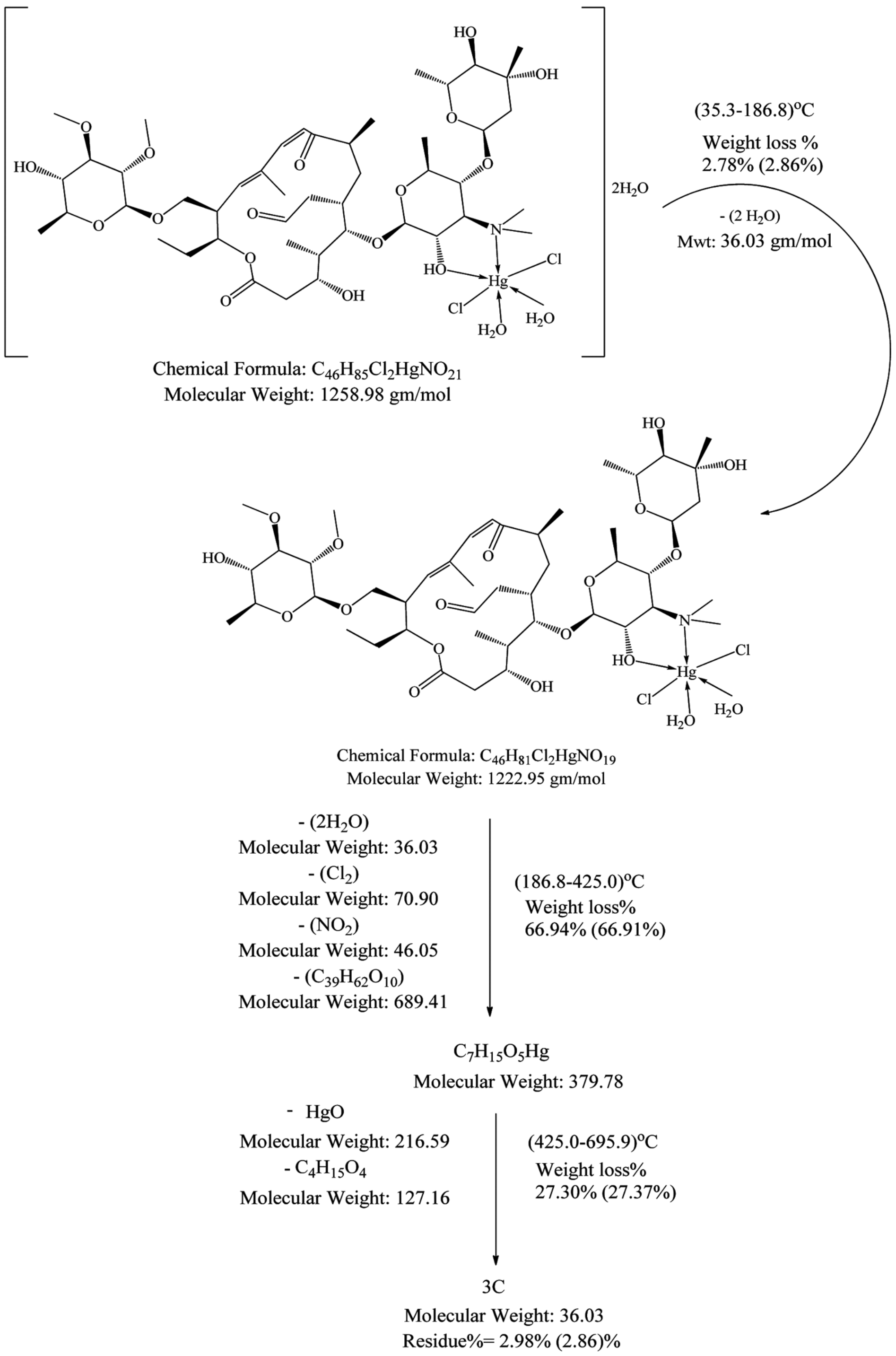


Fig. 6 — TG/DTA curves of $[Hg(TYS)Cl_2(H_2O)_2]\cdot 2H_2O$ complex

groups carry high electronegative charge confirming active sites for coordination. The oxygen and nitrogen atoms did not carry more electronegative charge but, the dihedral angles for O(45)-C(25)-C(26)-N(42) is (–68.888°) pointed to the strong deviation from ideal actual angle (109.00°), which attributed to the distortion effect which leads to the most suitable coordination binding site of ligand. Generally, the dihedral angles 109.00° is very difficult to be the active coordinated site. So the distortion that occurred in the mycaminose fragment is expected to be the main reason which leads to formation of coordination bond between hydroxyl group and 3° amine group with different metal ions. This theoretical approach by using Gaussian 09 software matched with the experimental data which comes from different spectral studies and elemental analysis.

Quantum chemical studies of Tylan (tylosin A) ligand and its metal complexes.

It was noticed that metallic chelation makes the organic moiety more lipophilic. In reality, ligands may actually increase their bioactivity profiles by coordination, whilst some inactive ligands may acquire therapeutic qualities. As a result, they have emerged as a crucial of structure-selective binding agents for nucleic acids[27]. Quantum chemical parameters as global hardness (η) and softness (σ) are important measured parameters to predict the molecular stability and reactivity of ligand and new synthesized complexes[28]. By monitoring the values of the hardness in the Table 6 showed that these metal complexes $[Hg(TYS)Cl_2(H_2O)_2]$ and $[Cd(TYS)Cl_2\,(H_2O)_2]$ are less harder than its ligand tylosin A, this means that both mentioned complexes have the largest potential chemical resistance to change the number of electrons among the other molecules. Also, the values of softness as summarized in the Table 6 showed that both complexes have higher value of global softness which indicated that these complexes showed greater reactivity than its ligand. A low value of hardness means high softness which lead the complex to be highly reactive. A lower value of the energy gap ΔE makes these two complexes more reactive (low kinetic stability) than tylosin A ligand. The computed electrophilicity indexes gave a measure of the stabilization in energy when the system acquires an additional electronic charge from the environment and also toxicity of various pollutants[29,30]. From the electrophilicity index, (ω) values indicated that $[Cd(TYS)Cl_2(H_2O)_2]$ have the highest value of electrophilicity (6.86 eV), which shows high ability to accept electrons (the most reactive compound). Tylosin exhibits a strong antibacterial effect[31] and compares favourably to



Scheme 2 — Steps of $[Hg(TYS)Cl_2(H_2O)_2]\cdot 2H_2O$ thermal cracking

the Cd(II) complex, therefore the higher computed electrophilicity values suggested that this complex may also have potent antibacterial properties.

Highest occupied molecular orbital **(E_{HOMO})**, lowest unoccupied molecular orbital energy **(E_{LUMO})**, energy gap **(ΔE)**, electronegativity **(χ)**, chemical potential **(μ)**, global hardness **(η)**, softness **(σ)**, ionization potential **(I)**, electron affinity **(A)**, Electrophilicity index **(ω)**.

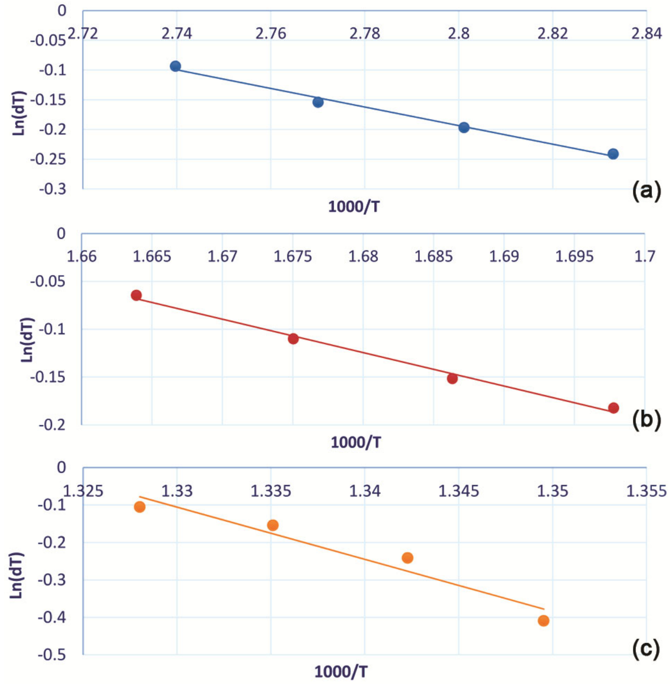


Fig. 7 — Relation of ln ΔT against 10^3/T for $[Hg(TYS)Cl_2(H_2O)_2]^{\cdot}2H_2O$, A (peak 1), B (peak 2) and C (peak3)

Table 4 — DTA Parameters of $[Hg(TYS)Cl_2(H_2O)_2]^{\cdot}2H_2O$ complex

Parameters	$[Hg(TYS)Cl_2(H_2O)_2]^{\cdot}2H_2O$ complex		
	Peak (1)	Peak (2)	Peak (3)
Type	Endo.	Exo.	Exo.
T_{max}(°K)	367.2	603.2	675.8
n	1.36	1.11	1.90
ΔE ($KJ.mol^{-1}$)	12.990	29.039	115.89
α_m	0.57	0.61	0.50
$\Delta S^{\neq}$ ($KJ.K^1mol^{-1}$)	–0.28	–0.30	–0.29
$\Delta H^{\neq}$ ($KJ.mol^{-1}$)	–27.18	–99.96	–118.63
Z (S^{-1})	0.016	0.010	0.034
Temperature range (°C)	35.3- 186.8	186.8- 425.0	425.0- 695.9
TGA			
Weight loss% Calc. (%)	2.78	66.94	27.30
Found (%)	2.86	66.91	27.37
Assignment	- Assumed to removal of outer water molecules.	- Assigned to removal of two coordinated water and NO_2 - Loss of $C_{39}H_{62}O_{10}$ from the bulky complex structure	- elimination of one molecule HgO mainly with residue of three carbon atoms

Table 5 — Selected charge density, bond lengths, bond angles and dihedral angles for optimized structure of tylosin A ligand atoms

Charge density	Bond length (Å)	Bond angles (°)	Dihedral angles (°)
O(10) Carbonyl -0.601878	C(26)-N(42) 1.438	N(42)-C(44)-H(112) 110.605	O(45)-C(25)-C(26)-H(90) 60.475
O(19) Carbonyl -0.632549	N(42)-C(43) 1.438	N(42)-C(44)-H(113) 112.339	O(45)-C(25)-C(26)-C(27) 174.495
O(20) Carboxyl -0.130786	N(42)-C(44) 1.438	N(42)-C(44)-H(114) 112.602	O(45)-C(25)-C(26)-N(42) -68.888

(*contd.*)

Table 5 — Selected charge density, bond lengths, bond angles and dihedral angles for optimized structure of tylosin A ligand atoms

Charge density	Bond length (Å)	Bond angles (°)	Dihedral angles (°)
O(21) Alcohol -0.406352	C(25)-O(45) 1.401	N(42)-C(43)-H(109) 110.191	N(42)-C(26)-C(27)-H(91) -58.926
O(23) Ether -0.370842	O(45)-H(115) 0.961	N(42)-C(43)-H(110) 111.646	N(42)-C(26)-C(27)-C(28) -178.279
O(29) Ether -0.373801	O(23)-C(24) 1.391	N(42)-C(43)-H(111) 113.229	N(42)-C(26)-C(27)-O(31) 62.773
O(31) Ether -0.369185	C(14)-O(23) 1.382	N(42)-C(26)-C(25) 109.119	H(89)-C(25)-C(26)-N(42) 64.190
O(37) Ether -0.366522	C(34)-O(41) 1.394	N(42)-C(26)-C(27) 119.172	C(24)-C(25)-C(26)-N(42) -174.407
O(39) Alcohol -0.382492	C(27)-O(31) 1.382	N(42)-C(26)-H(90) 106.952	C(44)-N(42)-C(43)-H(111) -54.525
O(41) Alcohol -0.390169	C(18)-O(19) 1.208	C(26)-N(42)-C(43) 114.079	C(44)-N(42)-C(43)-H(110) -177.694
N(42) Amine -0.128883	–	C(26)-N(42)-C(44) 114.768	C(44)-N(42)-C(43)-H(109) 64.722
O(45) Alcohol -0.391725	–	C(43)-N(42)-C(44) 110.065	–
O(48) Carbonyl -0.445214	–	C(25)-O(45)-H(115) 108.752	–
O(52) Ether -0.358639	–	O(45)-C(25)-C(24) 109.970	–
O(58) Ether -0.372065	–	O(45)-C(25)-C(26) 108.094	–
O(60) Alcohol -0.383765	–	O(45)-C(25)-H(89) 107.507	–
O(61) Ether -0.333396	–	–	–
O(63) Ether -0.337998	–	–	–
O(39) Alcohol -0.382492	–	–	–

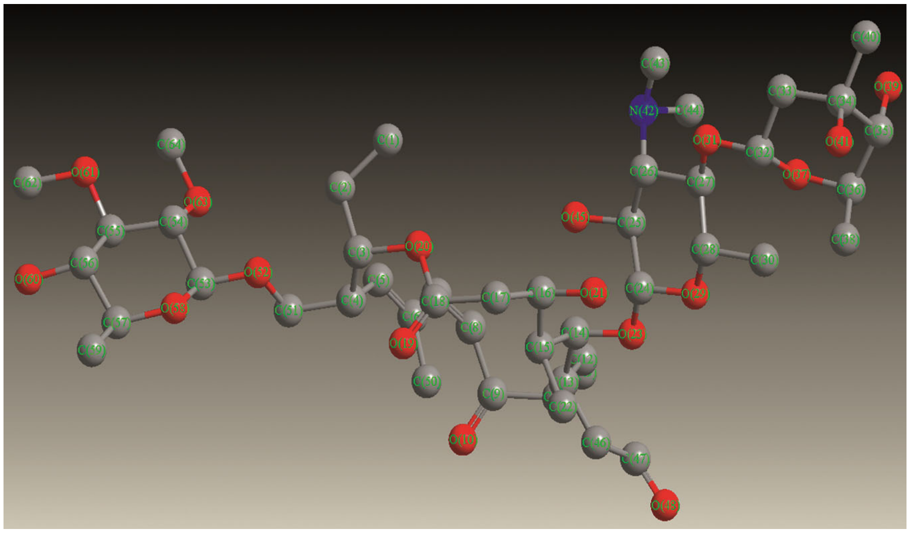


Fig. 8 — Optimized geometry of tylosin A ligand calculated with the B3LYP/6-311+G(d,p)

Table 6 — Quantum chemical parameters (eV) of Tylosin A and its metal complexescalculated by PM3 method.

Compd	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)	I (eV)	A (eV)	χ (eV)	μ (eV)	η (eV)	σ (eV)	ω (eV)
Tylan (Tylosin A)	–9.17	–2.00	7.17	9.17	2.00	5.58	–5.58	3.58	0.28	4.35
$[Hg(TYS)Cl_2(H_2O)_2]$	–8.24	–1.79	6.45	8.25	1.80	5.02	–5.02	3.22	0.31	3.91
$[Cd(TYS)Cl_2(H_2O)_2]$	–7.17	–3.23	3.94	7.17	3.23	5.20	–5.20	1.97	0.51	6.86

Conclusion

The preparation and characterization of the metal complexes of TYS with Cd (II) and Hg (II) were presented. The existence of these complexes has been confirmed by FTIR spectroscopy, which revealed that formation of these complexes occurred by chelation of metal ions through oxygen of OH group and nitrogen atom of mycaminose amine sugar. Further, the formed complexes have been in 1:1 stoichiometry of TYS and each studied metal. The molecular modeling data including charges, bond lengths, bond angles and dihedral angles of the ligand were calculated that confirmed the suggested structure of both complexes formed. The follow-up of the pathway of the thermal decomposition and final residues confirmed the chemical formula and geometrical structure of the prepared metal complexes. The first decomposition step corresponds to dehydration of water molecules and loss of small molecules. The thermal decomposition reactions ended with the formation of carbon or metal oxide contaminated with carbon sometimes. The activation thermodynamic parameters, such as activation energy (ΔE*), enthalpy of activation (ΔH*), entropy of activation (ΔS*) and Gibbs energy (ΔG*) have been calculated using DTA curve. Quantum chemical parameters predicted that the novel complexes may possess biological activity by comparing values of electrophilicity index, (ω) of ligand and its new metal complexes.

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