

Synthesis, spectral characterization, *in vitro* microbial and cytotoxic studies of lanthanum(III) and thorium(IV) complexes with 1,2,4-triazole Schiff bases

GANGADHAR B. BAGIHALLI¹, SANGAMESH A. PATIL¹, & PREMA S. BADAMI²

¹*P.G. Department of Chemistry, Karnatak University, Dharwad 580003, Karnataka, India, and* ²*Department of Chemistry, Shri Sharanabasaveswar College of Science, Gulbarga 585102, Karnataka, India*

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Abstract

A series of metal complexes of La(III) and Th(IV) have been synthesized with newly derived biologically active ligands. These ligands were synthesized by the condensation of 3-substituted-4-amino-5-hydrazino-1,2,4-triazole with 8-formyl-7-hydroxy-4-methylcoumarin. The structure of the complexes has been proposed by elemental analyses, spectroscopic data i.e. i.r., ¹H nmr, Uv-Vis, FAB-mass and thermal studies. The elemental analyses of the complexes conform to the stoichiometry of the type [La(L)·3H₂O]·2H₂O and [Th(L)(NO₃)·2H₂O]·2H₂O where (L = L^I-L^{IV}). All the complexes are soluble in DMF and DMSO and are non-electrolytes in DMF and DMSO. All these ligands and their complexes have also been screened for their antibacterial (*Escherichia coli*, *Staphylococcus aureus*, *Staphylococcus pyogenes* and *Pseudomonas aeruginosa*) and antifungal activities (*Aspergillus niger*, *Aspergillus flavus* and *cladosporium*) by the MIC method. The brine shrimp bioassay was also carried out to study their invitro cytotoxic properties.

Keywords: Synthesis, biological activity, cytotoxic, 1,2,4-triazole, coumarin, La(III) and Th(IV) complexes

Introduction

Schiff base complexes with transition metals have played a prominent role in the development of coordination chemistry [1,2]. Synthesis of 1,2,4-triazole derivatives has attracted widespread attention due to their diverse biological activities. Triazole derivatives [3–6] are known to possess antibacterial, fungicidal, hypotensive and hypothermic activities. In addition to 1,2,4-triazole derivatives coumarin derivatives display an additional significant biological [7–11] and pharmacological [12,13] properties. Many of these compounds possess antibacterial [12], antifungal [13] and insecticidal [10] activities and the hydroxycoumarins are the typical phenolic compounds and therefore, act as potent metal chelators and free radical scavengers. They are powerful chain-breaking anti-oxidants [14]. Metal complexes of 1,2,4-triazole

derivatives have been extensively investigated and reported from our laboratory [15–18].

Recently, a number of attempts have been made to obtain Co(II), Ni(II), Cu(II) and Zn(II) complexes with the Schiff bases derived from cinnamaldehyde and 4-amino-3-ethyl-5-mercapto-s-triazole and 4-amino-5-mercapto-3-n-propyl-s-triazole [19] and cobalt(II), Nickel(II) and copper(II) complexes with Schiff base derived from furfuraldehyde and 3-substituted-4-amino-5-mercapto-s-triazole have been isolated and characterized by elemental analyses, magnetic, spectral (IR, Uv-Vis, EPR) and thermal studies [20].

In continuation of our efforts on 1,2,4-triazole derivatives we have synthesized a new series of Schiff bases derived from 3-substituted-4-amino-5-hydrazino-1,2,4-triazole and 8-formyl-7-hydroxy-4-methylcoumarin. The survey of the literature reveals that, no

Correspondence: S. A. Patil, P.G. Department of Chemistry, Karnatak University, Dharwad 580003, Karnataka, India.
E-mail: patil1956@rediffmail.com

work has been carried out on the synthesis of metal complexes with these Schiff bases. These ligands have donor sites with the ONNNO sequence and varied coordination abilities. Because of the importance of triazole and coumarin compounds in biological and medicinal fields and also the La(III) and Th(IV) complexes are well reported as antimicrobial and cytotoxic effect with coumarin derivatives [21–23]. Thus, it attracted our attention and aroused our interest in elucidating the structure of La(III) and Th(IV) complexes with these bioactive Schiff bases (Figure 1). The Schiff base metal complexes are characterized by spectral, thermal and molar conductance studies and these are evaluated for their antibacterial and antifungal properties against various pathogenic bacterial strains using the minimum inhibitory concentration (MIC) method.

Material and methods

All the chemicals used were of reagent grade. 7-hydroxy-4-methyl-coumarin was obtained from Acros Chemical Company. 3-substituted-4-amino-5-mercapto-1,2,4-triazole was prepared as described in the literature [24,25]. The IR spectra of the Schiff bases and their La(III) and Th(IV) complexes were recorded on a HITACHI-270 IR spectrophotometer in the 4000–250 cm^{-1} region in KBr disks. The electronic spectra of the complexes were recorded in DMF on a VARIAN CARY 50-BIO UV-spectrophotometer in the region of 200–1100 nm. The proton NMR spectra of ligands and its metal complexes were recorded in CDCl_3 on a BRUKER 300 MHz spectrometer at room temperature using TMS as an internal reference. FAB mass spectra were recorded on a JEOL SX 102/DA-6000 mass spectrometer/data system using Argon/Xenon (6 KV, 10Am) as the FAB gas. The accelerating voltage was 10 KV and the spectra were recorded at room temperature *m*-nitrobenzyl alcohol was used as the matrix. The mass spectrometer was operated in the positive ion mode. Particle size was measured by Zetasizer technique, Model 3000HS, Malvern, U.K. Thermogravimetric analysis data were measured from room

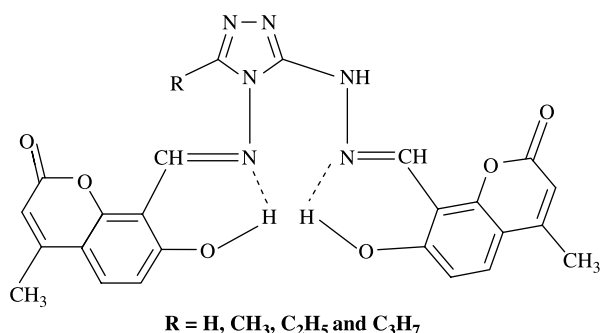


Figure 1. Synthesized Schiff bases.

temperature to 1000°C at a heating rate of 10°C/min. The data were obtained by using a PERKIN-ELMER DIAMOND TG/DTG instrument. Molar conductivity measurements were recorded on a ELICO-CM-82 T conductivity bridge with a cell having cell constant 0.51 and magnetic moment was carried out on faraday balance.

Synthesis of 3-substituted-4-amino-5-hydrazino-1,2,4-triazole

A mixture of 3-substituted-4-amino-5-mercapto-1,2,4-triazole and $\text{N}_2\text{H}_4 \cdot \text{H}_2\text{O}$ in 1:1 molar proportions in EtOH was boiled under reflux for 4–5 h on a water bath. The reaction mixture was cooled at room temperature; within 1 h the compound separated from the clear solution. It was filtered, washed and recrystallized from EtOH.

Synthesis of Schiff bases (L^I – L^{IV})

A mixture of 3-substituted-4-amino-5-hydrazino-1,2,4-triazole and 8-formyl-7-hydroxy-4-methylcoumarin [26] in 1:1 molar proportion in an alcoholic medium containing few drops of concentrated HCl was refluxed for 3–4 h. The product separated is filtered, washed with alcohol and was recrystallized from EtOH.

Synthesis of La(III) complexes (1–4)

The lanthanum(III) nitrate (0.01 mol) in super-dry alcohol was treated with (0.01 mol) ligand in super-dry alcohol. The reaction mixture was boiled under reflux for 2–3 h. After cooling, the pH of the reaction mixture was adjusted to *ca.* pH 7 by adding dilute ammonia with constant stirring. The dark green precipitate of the complexes was filtered, washed thoroughly with dry alcohol and ether and finally dried over fused CaCl_2 in vacuum.

Synthesis of Th(IV) complexes (5–8)

Thorium(IV) nitrate (0.01 mol) was boiled under reflux with the ligand (0.01 mol) in alcohol for 3 h. The complex was precipitated by adding distilled water containing liquor ammonia. The precipitated complex was filtered, washed thoroughly with distilled water, alcohol then with ether, and dried under reduced pressure over fused CaCl_2 .

In vitro antibacterial and antifungal assay

The synthesized Schiff bases and their corresponding La(III) and Th(IV) complexes were screened for their biological activity by using five bacteria, namely *E. coli*, *S. aureus*, *S. pyogenes*, *Salmonella typhi* and

P. aeruginosa and three fungi namely *A. niger*, *A. flavus* and *cladosporium* by the reported method [27,28].

The bacteria were subcultured in agar medium. The petridishes were incubated for 24 h at 37°C. Standard antibacterial drug (gentamycine) was also screened under similar conditions for comparison. The fungi were subcultured in potato dextrose agar medium. Standard antifungal drug (fluconazole) was used for comparison. The petridishes were incubated for 48 h at 37°C. The wells were dug in the agar media using a sterile metallic borer. Activity was determined by measuring the diameter of the zone showing complete inhibition (mm). Growth inhibition was compared with the standard drugs. In order to clarify any effect of DMF on the biological screening, separate studies were carried out with solutions alone of DMF and they showed no activity against any microbial strains. The stock solution (1 mg mL⁻¹) of the test chemical was prepared in DMF.

Minimum inhibitory concentration (MIC)

Some compounds showing promising antibacterial/antifungal activity were selected for minimum inhibitory concentration studies [29,30].

In vitro cytotoxicity

The synthesized Schiff base and its La(III) and Th(IV) complexes were screened for their cytotoxicity (brine shrimp bioassay) using protocol of Meyaer [31]. Brine shrimp (*Artemia salina* leach) eggs were hatched in a shallow rectangular plastic dish (22 × 32 cm) filled with artificial seawater, which was prepared with a commercial salt mixture and double distilled water. An unequal partition was made in the plastic dish with the help of a perforated device. Approximately 50 mg of eggs were sprinkled into the large compartment, which was darkened while the minor compartment was open to ordinary light.

After two days, nauplii were collected by a pipette from the lighted side. A sample of the test compound was prepared by dissolving 20 mg of each compound in 2 mL of DMF. From this stock solutions 100, 50 and 10 µg/mL were transferred to 9 vials (three for each dilutions were used for each test sample and LD₅₀ is the mean of three values) and one vial was kept as control having 2 mL of DMF only. The solvent was allowed to evaporate overnight. After two days, when shrimp larvae were ready, 1 mL of seawater and 10 shrimps were added to each vial (30 shrimps/dilution) and the volume was adjusted with seawater to 5 mL per vial. After 24 h the number of survivors was counted. Data were analyzed by a finney computer program to determine the LD₅₀ values [32].

Results and discussion

All the La(III) and Th(IV) complexes are colored, stable in air and non-hygroscopic solids. They are soluble in DMF and DMSO. The elemental analyses show that, the La(III) and Th(IV) complexes have 1:1 stoichiometry. The molar conductance values at the 10⁻³M concentration are too low to account for any dissociation of the complex in DMF. Hence, the La(III) and Th(IV) complexes may be regarded non-electrolytes. In order to establish whether the water molecules present in the complexes coordinated to the metal ion, weighed complexes were dried in over P₂O₅ in a vacuum for *ca* 1 h. and then weighed again. No loss in weight was observed. These observations suggest the water molecules in the complexes are coordinated to the metal ion. The metal contents were estimated gravimetrically by the standard method [33]. Carbon, hydrogen, nitrogen and sulphur were estimated by using C, H, N and S analyzer. The results of elemental analyses and molar conductance values are listed in Table I.

Table I. Elemental analysis and molar conductance data of Schiff bases (I-IV) and their La(III) and Th(IV) complexes (1-8).

No.	Empirical formula	M%		C%		H%		N%		Molar conductance Ohm ⁻¹ cm ⁻² mole ⁻¹
		Obsd.	Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	Obsd.	Calcd.	
I	C ₂₄ H ₁₈ N ₆ O ₆ (L ^I)	–	–	59.20	59.26	3.66	3.70	17.24	17.28	–
II	C ₂₅ H ₂₀ N ₆ O ₆ (L ^{II})	–	–	59.93	60.00	3.95	4.00	16.77	16.80	–
III	C ₂₆ H ₂₂ N ₆ O ₆ (L ^{III})	–	–	60.64	60.70	4.21	4.28	16.30	16.34	–
IV	C ₂₇ H ₂₄ N ₆ O ₆ (L ^{IV})	–	–	61.31	61.36	4.52	4.55	15.88	15.91	–
1	[La(L ^I)·3H ₂ O]·2H ₂ O	19.47	19.51	40.40	40.45	2.08	2.11	11.75	11.79	28
2	[La(L ^{II})·3H ₂ O]·2H ₂ O	19.11	19.14	41.28	41.33	2.31	2.34	11.52	11.57	25
3	[La(L ^{III})·3H ₂ O]·2H ₂ O	18.71	18.77	42.13	42.17	2.52	2.57	11.31	11.36	22
4	[La(L ^{IV})·3H ₂ O]·2H ₂ O	18.39	18.43	42.95	42.98	2.76	2.79	11.10	11.14	20
5	[Th(L ^I)(NO ₃)·2H ₂ O]·2H ₂ O	27.30	27.33	33.89	33.92	1.72	1.76	11.49	11.54	19
6	[Th(L ^{II})(NO ₃)·2H ₂ O]·2H ₂ O	26.95	26.99	34.73	34.76	1.92	1.96	11.30	11.36	18
7	[Th(L ^{III})(NO ₃)·2H ₂ O]·2H ₂ O	26.40	26.45	35.52	35.57	2.11	2.16	11.11	11.17	20
8	[Th(L ^{IV})(NO ₃)·2H ₂ O]·2H ₂ O	26.00	26.04	36.31	36.36	2.31	2.36	10.94	10.99	24

Table II. Important infrared frequencies (cm⁻¹) of 3-substituted-4-amino (8-formyl-7-hydroxy-4-methylcoumarin)-5-hydrazino-1,2,4-triazole Schiff bases.

Ligand No.	ν (NH)	Lactone ν (C=O)	ν (C=N)	H-bonded -OH Stretching	ν (C=C)	Phenolic ν (C-O)
I	3130 brm 3071 m	1700	1625	2758	1590	1279
II	3125 brm 3068 m	1707	1630	2750	1600	1285
III	3115 brm 3058 m	1705	1615	2755	1595	1292
IV	3120 brm 3065 m	1710	1620	2752	1597	1294

IR spectra

The important IR frequencies of the Schiff bases and their La(III) and Th(IV) complexes are listed in the Tables II and III respectively.

In the IR spectra of Schiff bases a medium band appeared in the region 3130-3058 cm⁻¹ due to ν (NH). A medium of high intensity band *ca* 1630-1615 cm⁻¹ was assigned to ν (C=N) so confirming coumarin residues.

In addition to the above, a broad weak band with fine structure in the region 2758-2750 cm⁻¹ and that can be attributed to the intramolecular H-bonded-OH. Medium intensity bands in the 1610-1590 cm⁻¹ region are regarded as a combination of C=N of triazole ring and aromatic C=C stretching vibrations. A high intensity band is present in the 1295-1279 cm⁻¹ region with an additional band in the region *ca* 1600-1590 cm⁻¹ was assigned to the phenolic ν (C-O) vibrations. The band located at 1715-1700 cm⁻¹ in all these Schiff bases attributed to ν (C=O) [34].

In the complexes we observed the following changes.

The disappearance of medium band appeared in the region 3130-3058 cm⁻¹ of the Schiff bases due to ν (NH) in the La(III) and Th(IV) complexes, supports the formation of M-N bands via deprotonation. So the H atoms of -NH group have been replaced by the metal ion. The characteristic band due to ν (C=N) appears in the region *ca* 1611-1603 cm⁻¹ for these La(II) and Th(IV) complexes. The low frequency shift of ν (C=N) band suggesting that, the C=N group is coordinated to the metal ion through nitrogen and this has resulted in lowering of the bond order of carbon to nitrogen link. The high intensity

band due to phenolic C-O appeared in the region 1295-1285 cm⁻¹ in the Schiff bases appeared as a medium to high intensity band in the 1380-1392 cm⁻¹ region in the complexes. These observations support the formation of M-O bands via deprotonation. So the H atoms of -OH groups have been replaced by the metal ion [35].

All these complexes exhibit a broad through band in the region 3422-3442 cm⁻¹ indicates the presence of lattice or coordinated water molecule [36] and the additional two weaker bands in the region 800-750 and 720-700 cm⁻¹ due to ν (-OH) rocking and wagging mode of vibrations, confirms the presence of coordinated water in all La(III) and Th(IV) complexes [37]. The medium intensity band in the region *ca* 555-537 cm⁻¹ is characteristic of ν (M-O) vibration of the phenolic oxygen and the coordinated water molecules [38] and a band at *ca* 492-480 cm⁻¹ is due to ν (M-N) modes [39].

In the infrared spectra of Th(IV) complexes, the two bands associated with asymmetric stretch appear around 1440 and 1270 cm⁻¹, the magnitude of separation between these two is *ca* 170 cm⁻¹, typical of bidentate bonding of nitrates. The band located at 1715-1700 cm⁻¹ due to ν (C=O) in the Schiff bases are unaffected in the complexes indicating that the lactone Oxygens are not involved in the coordination.

¹H NMR spectra

The ¹H NMR spectra of Schiff bases exhibit signals at 13.58, 10.21, 8.62 and 7.2-7.5 ppm due to -NH, phenolic OH, -CH=N and aromatic protons respectively. The signals around 2.84 ppm are due to methyl protons.

Table III. Important infrared frequencies (cm⁻¹) of La(III) and Th(IV) complexes (1-8).

Complex No.	ν (OH)	ν (C=N)	ν CH ₃	Phenolic C-O	ν (M-N)	ν (M-O)
1	3435	1604	2930	1385	485	542
2	3422	1600	2928	1392	491	537
3	3440	1603	2922	1380	489	548
4	3438	1610	2940	1386	480	539
5	3425	1609	2915	1390	490	555
6	3437	1607	2930	1384	483	543
7	3439	1600	2928	1386	492	542
8	3442	1611	2927	1389	485	550

In case of the La(III) and Th(IV) complexes we observed the following changes.

The signal due to azomethine proton of Schiff bases (*ca* 8.62 ppm) shows a downfield shift *ca* 9.21 ppm [40] in the spectra of complexes indicating the coordination of the azomethine group to the metal ion through metal ion. This downfield shift is due to deshielding of the =CH proton. All these observations supported the IR inferences. The resonance due to phenolic –OH *ca* 10.21 ppm disappears in the spectrum of complexes; this confirms that, the hydroxyl group reacted with metal ion via deprotonation. The resonance due to –NH *ca* 13.58 ppm disappears in the spectrum of complexes, indicating the coordination of the amine group to the metal ion. The signal due to water protons in the complexes appears *ca* 5.45 ppm. All these observations support the structure suggested by IR.

The signal due to a multiplet *ca* 7.7–7.8 ppm due to aromatic protons and signals around 2.84 ppm due to methyl protons are unaffected in the case of metal complexes.

¹³C NMR spectrum

The ¹³C NMR spectrum of Schiff base (II) exhibits the signals at 117.4, 119.2, 120.4, 128.1, 135.0 and 149.2 ppm are corresponding to aromatic carbons. The resonance at 11.6 ppm is due to aliphatic (–CH₃) carbon and the azomethine (–HC=N) carbon shows peak at 159.2 ppm.

Electronic absorption spectra

The electronic absorption spectra of the complexes were recorded for freshly prepared solutions in DMF, DMSO, THF and MeCN at room temperature. These complexes exhibited a broad band *ca* 31000 cm^{–1} which was assigned to L → M charge transfer transition.

Magnetic studies

As expected all of these complexes are diamagnetic

FAB mass spectrum of Schiff base (II) and its La(III) (2) and Th(IV) complex (6)

The FAB spectrum of Schiff base (II) showed a molecular ion peak at *m/z* 500 which is equivalent to its molecular weight. The fragments in the spectrum leading to the formation of the species [C₂₅H₂₀N₆O₆]⁺. The FAB mass spectrum of La(III) (2) (Figure 1S) complex shows a molecular ion peak M⁺ at *m/z* 726 which is equivalent to its molecular weight of the La(III) (2) complex. This molecular ion undergoes fragmentation with the loss of three water molecules, gave a fragment ion [La(L^{II})]·2H₂O at *m/z*

672. This molecular ion gave the fragment ion [La(C₂₂H₁₄N₃O₆)·3H₂O] at *m/z* 610 by the loss of triazole (C₃H₃N₃) and two lattice held water molecules. Finally it undergoes dematallation to form the species [L^{II} + H]⁺ gave a fragment ion at *m/z* 498. All these fragmentation patterns are well observed in the FAB mass spectrum.

In case of the Th(IV) (6) (Figure 2S) complexes, the spectrum shows a molecular ion peak M⁺ at *m/z* 863, which is equivalent to its molecular weight [Th(L^{II})(NO₃)·2H₂O]·2H₂O. This species by the loss of two water molecules gave a fragment ion [Th(L^{II})(NO₃)·2H₂O] at *m/z* 827. This fragment ion lost the one nitrate molecules and gave a fragment ion [Th(L^{II})]·2H₂O at *m/z* 765. Finally, it undergoes dematallation to form the species [L^{II} + H]⁺ gave a fragment ion at *m/z* 498.

Thermogravimetric analyses

TG and DTG studies were carried out for La(III) (2) and Th(IV) (6) complexes. These complexes decompose gradually with the formation of respective metal oxide above 600°C shown in Figures 3S and 4S. The nature of proposed chemical change with the temperature range and the percentage of metal oxide obtained are given in the Table IS. The thermograms of these complexes show initial weight loss in the temperature range 75–98°C is evidence for the presence of water molecules. The loss of water molecules in this temperature range indicates that they are present as lattice-held water [41]. The percentage weight loss in this temperature range indicates that there are two to three water molecules each in all these complexes as lattice water. The second stage loss of water molecules in the range of 225–250°C in these complexes correspond to the loss of water molecules in coordinated sphere. The third stage of decomposition of all these complexes in the range of 475–520°C is corresponds to the loss of organic moiety and the final weight corresponded to that of the metal oxide.

Kinetic study

The Freeman and Corroll procedure [42] was used to evaluate the kinetic parameters such as order of reaction and energy of activation from a single experimental curve from the plot of $\frac{\Delta \log \frac{dw}{dt}}{\Delta \log W_r}$ versus $\frac{\Delta T^{-1}}{\Delta \log W_r} \times 10^3 \text{K}^{-1}$. The determined order of reaction and energy of activation are listed in Table IIS.

Antimicrobial results

The microbial results are systematized in Tables IV and V and shown in Figures 2 and 3. In the case of bacteriological studies it was observed that, the ligand

Table IV. Antibacterial and antifungal activities of Schiff bases (I-IV).

Compd.	Conc. ($\mu\text{g mL}^{-1}$)	Antibacterial activity (Zone of inhibition in %)				Antifungal activity (Zone of inhibition in %)		
		<i>E. coli</i>	<i>S. aureus</i>	<i>S. pyogenes</i>	<i>P. aeruginosa</i>	<i>A. flavus</i>	<i>Cladosporium</i>	<i>A. niger</i>
L ^I	100	50	45	48	67	85	74	75
L ^{II}	100	58	59	52	60	88	82	78
L ^{III}	100	55	57	59	69	70	76	131
L ^{IV}	100	61	60	57	63	74	72	80
Standard	100	100	100	100	100	100	100	100

Standard = Gentamycine (antibacterial) and fluconazole (antifungal).

Table V. Antibacterial and antifungal activities of La(III) and Th(IV) complexes (1-8) and standards.

Compd.	Conc. ($\mu\text{g mL}^{-1}$)	Antibacterial activity (Zone of inhibition in %)				Antifungal activity (Zone of inhibition in %)		
		<i>E. coli</i>	<i>S. aureus</i>	<i>S. pyogenes</i>	<i>P. aeruginosa</i>	<i>A. flavus</i>	<i>Cladosporium</i>	<i>A. niger</i>
1	100	72	64	73	76	80	77	79
2	100	68	62	–	72	73	70	74
3	100	74	69	72	74	75	71	–
4	100	70	57	70	75	70	67	68
5	100	70	60	64	69	68	–	75
6	100	67	52	63	66	61	60	69
7	100	–	59	–	60	60	63	71
8	100	71	58	60	61	64	67	70
Standard	100	100	100	100	100	100	100	100

Standard = Gentamycine (antibacterial) and Fluconazole (antifungal).

shows moderate active toward *E. coli*, *P. aeruginosa* and *S. aureus* and low active towards *S. pyogenes*. Among the La(III) and Th(IV) complexes La(III) shows high activity towards *E. coli*, and *P. aeruginosa*. La(III) complexes show high active.

In case of antifungal activity it was observed that, the Schiff base shows high activity against *A. flavus*, *A. niger* and less active towards *Cladosporium*. In the case of La(III) complex, it shows high activity against

A. niger and *Cladosporium* and moderate active towards *A. flavus*, in case of *A. flavus* we got interesting result that it shows high activity.

It has been suggested that the ligands with nitrogen and oxygen donor systems inhibit enzyme activity, since the enzymes which require these groups of their activity appear to be especially more susceptible to deactivation by metal ions on coordination. Moreover, coordination reduces the polarity [31] of the metal ion

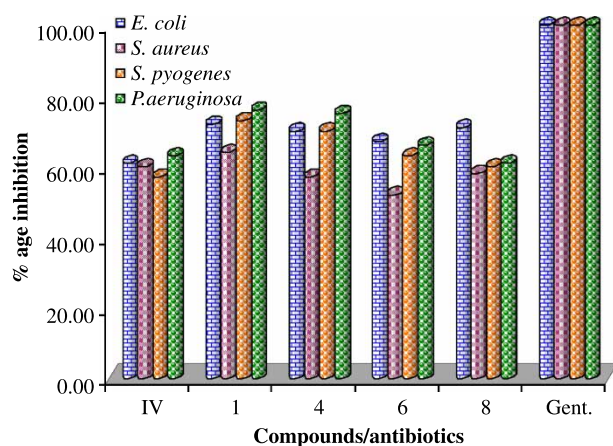


Figure 2. Antibacterial activity of Schiff base and its La(III) and Th(IV) complexes (100 $\mu\text{g/mL}$).

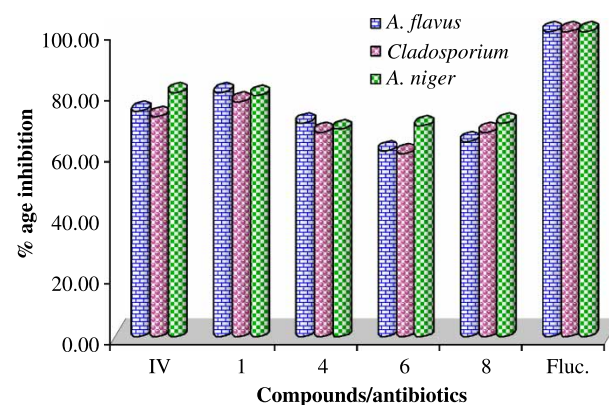


Figure 3. Antifungal study of Schiff base and its La(III) and Th(IV) complexes (100 $\mu\text{g/mL}$).

Table VI. Minimum inhibitory concentration ($\mu\text{g/mL}^{-1}$) for La(III) and Th(IV) complexes.

Compd.	Antibacterial activity				Antifungal activity		
	<i>E. coli</i>	<i>S. aureus</i>	<i>S. pyogenes</i>	<i>Paeruginosa</i>	<i>A. flavus</i>	<i>Cladosporium</i>	<i>A. niger</i>
1	10	20	15	10	15	20	20
2	15	20	–	15	20	20	15
3	10	20	15	15	15	15	–
4	15	25	15	10	10	15	20
5	10	15	25	25	25	–	15
6	20	25	25	25	30	30	25
7	–	20	–	30	30	25	20
8	15	20	30	30	30	25	25

Table VII. Brine shrimp bioassay data for the ligands (L^I - L^{IV}) and their metal (II) complexes 1-8.

Compound	LD_{50} (moles/mL)
L^I	4.517×10^{-3}
L^{II}	6.324×10^{-3}
L^{III}	5.842×10^{-3}
L^{IV}	6.247×10^{-3}
1	7.623×10^{-4}
2	6.459×10^{-3}
3	5.682×10^{-3}
4	8.945×10^{-4}
5	4.750×10^{-3}
6	7.839×10^{-3}
7	8.241×10^{-4}
8	5.135×10^{-3}

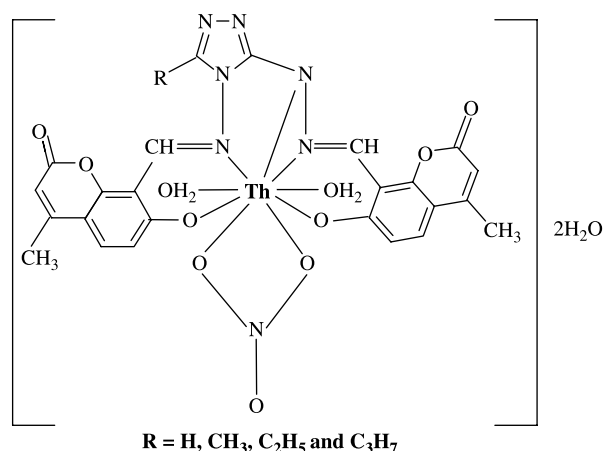


Figure 5.

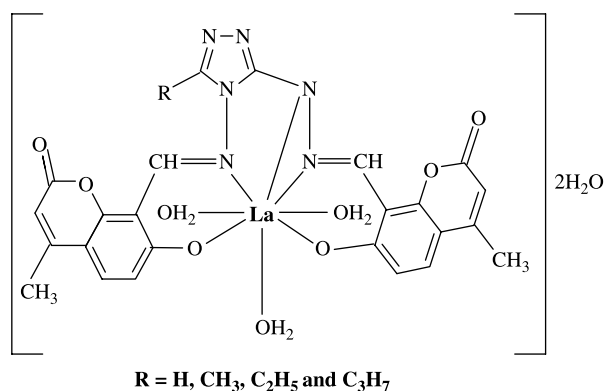


Figure 4.

mainly because of the partial sharing of its positive charge with the donor groups [43] with in the chelate ring system formed during coordination. This process, in turn, increases the lipophilic nature of the central metal atom, which favors its permeation more efficiently through the lipid layer of the micro-organism [44] thus destroying them more aggressively. The minimum inhibitory concentration $\mu\text{g/mL}^{-1}$ was shown by compounds ranging from 10-100 $\mu\text{g/mL}^{-1}$ against all the microbial strains are given in Table VI.

Cytotoxic bioassay

It is evident from the data recorded in Table VII that, only the complexes 1, 4, and 7 displayed cytotoxic activity as LD_{50} at c. 1×10^{-3} M against *Artemia salina*, while the Schiff bases and the remaining complexes were almost inactive for this assay.

Conclusion

The synthesized Schiff bases (I-IV) act as pentadentate ligands through the coordination of azomethine nitrogens, NH and phenolic oxygen atoms to the metal ion. The bonding of ligands to metal ion was confirmed by the analytical, i.e., ^1H nmr, Uv-Vis, FAB mass and thermal studies.

All Schiff bases were found potentially active towards all microbial strains and the La(III) and Th(IV) complexes show even more promising results than the Schiff bases.

All compounds are soluble in DMSO and DMF solvents. All these observations put together lead us to propose the structures shown in Figures 4 and 5 in which the complexes have the stoichiometry of the type $[\text{La}(\text{L})\cdot 3\text{H}_2\text{O}]\cdot 2\text{H}_2\text{O}$ and $[\text{Th}(\text{L})(\text{NO}_3)\cdot 2\text{H}_2\text{O}]\cdot 2\text{H}_2\text{O}$ where ($\text{L} = \text{L}^I$ - L^{IV}).

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Supplementary material

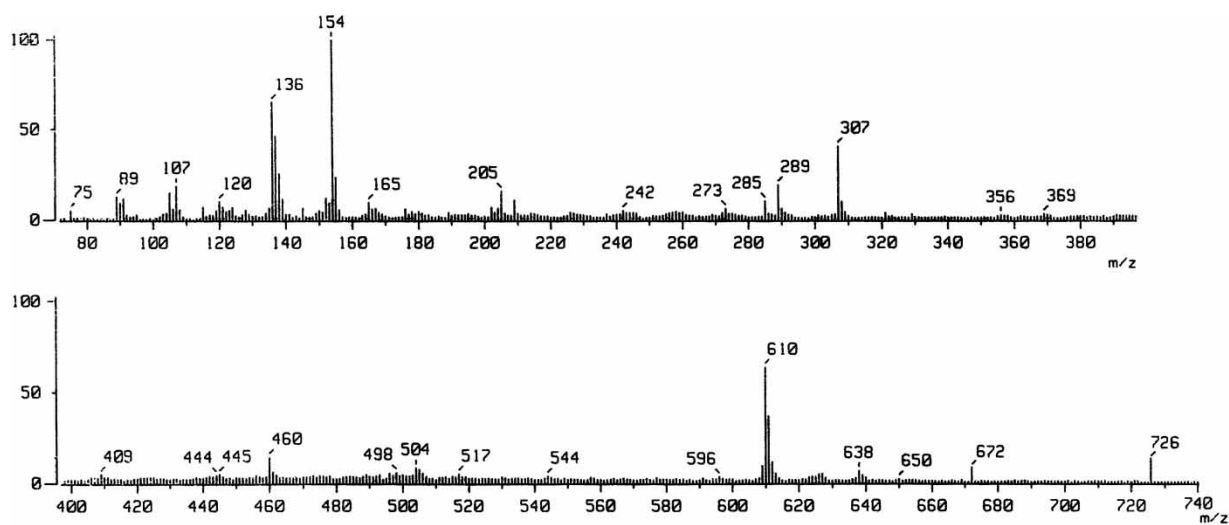


Figure 1S. FAB-mass spectrum of La(III) Complex.

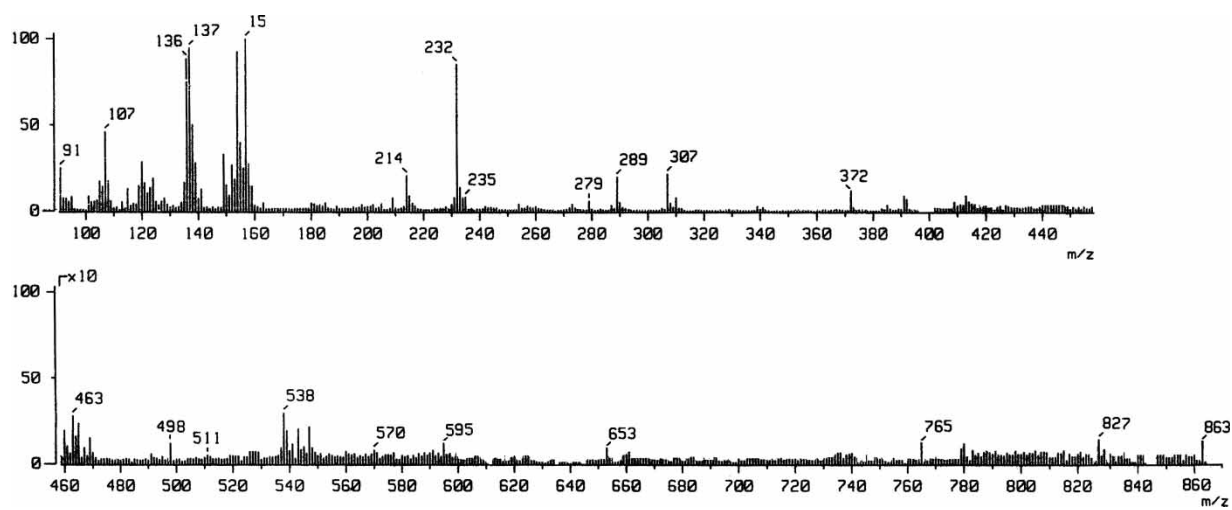


Figure 2S. FAB-mass spectrum of Th(IV) Complex.

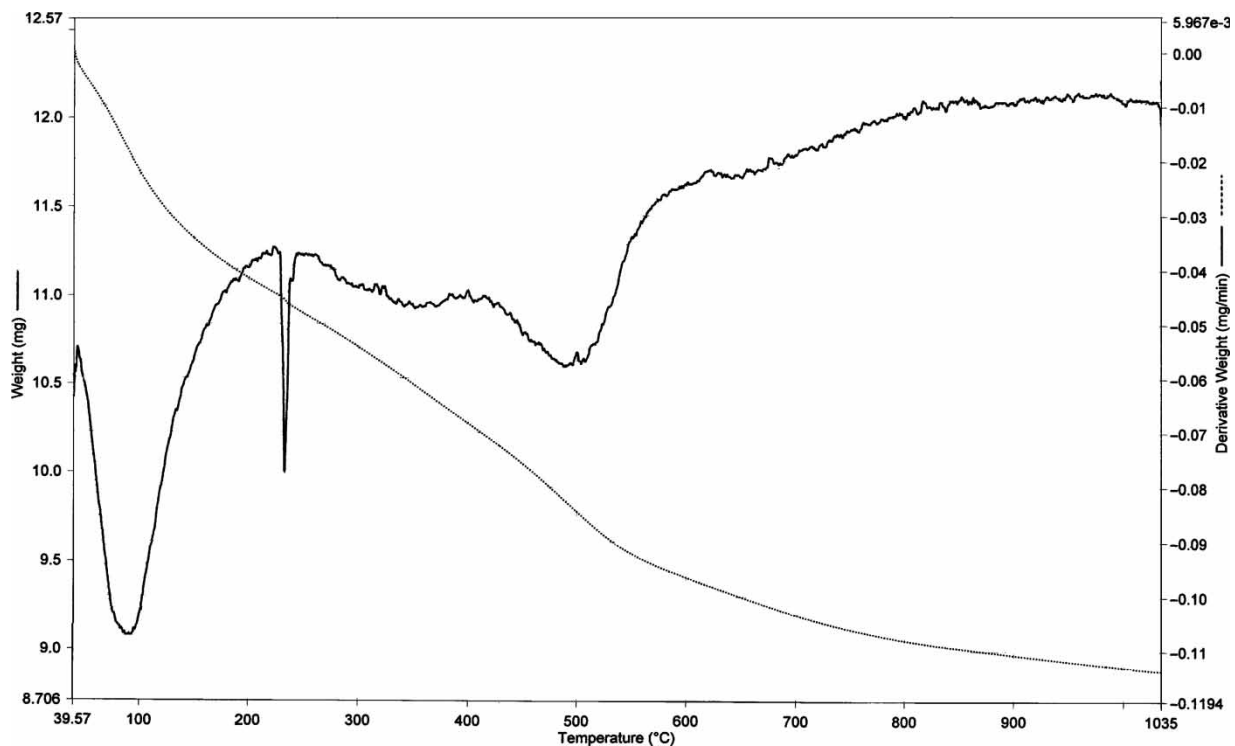


Figure 3S. Thermogravimetric (TGA/DTG) curves of La(III) complex (2).

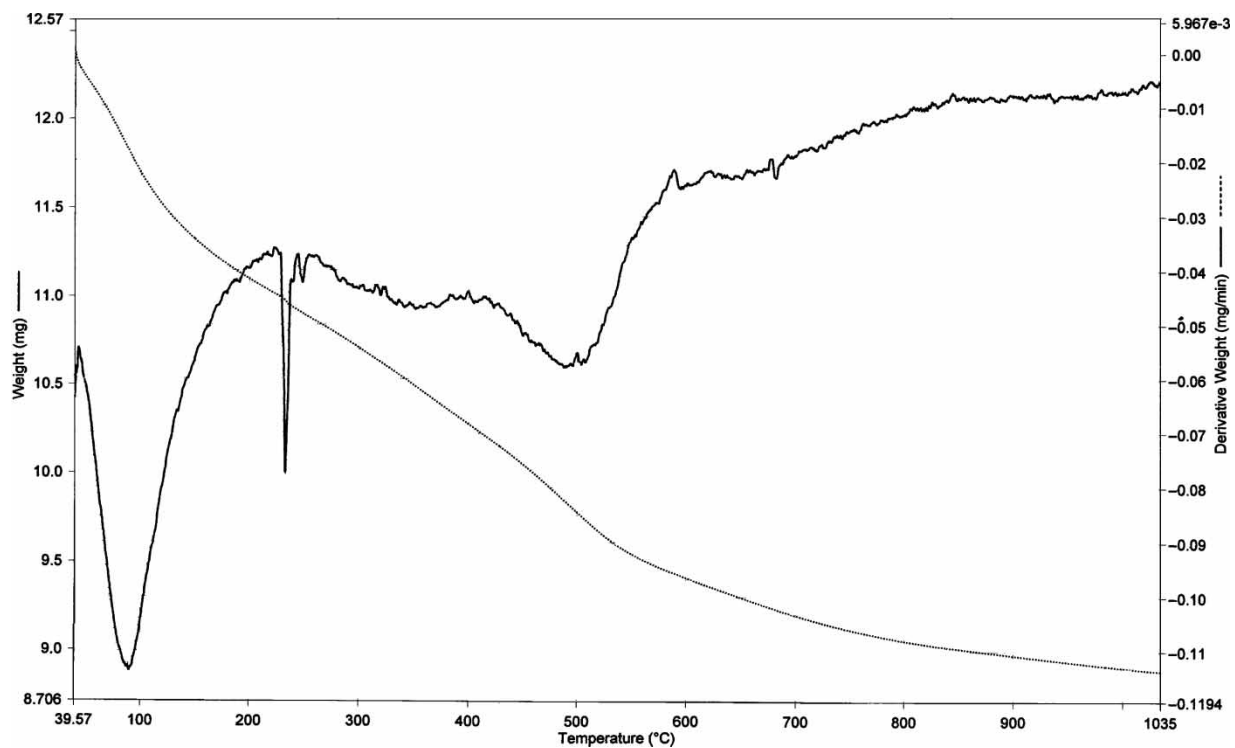


Figure 4S. Thermogravimetric (TGA/DTG) curves of Th(IV) complex (6).

Table IS. Thermogravimetric data for La(III) (2) and Th(IV) (6) complexes of 3-substituted-4-amino (8-formyl-7-hydroxy-4-methylcoumarin)-5-mercapto-1,2,4-triazole.

Empirical Formula	Decomposition temperature °C	%Weight loss		Inference
		Obsd.	Calcd.	
[La(L ^{II})·3H ₂ O]·2H ₂ O	080-097	4.90	4.96	Loss of lattice held water molecules
	230-250	7.39	7.44	Loss of coordinated water molecules
	475-515	68.82	68.88	Loss of organic moiety
[Th(L ^{II})(NO ₃)·2H ₂ O]·2H ₂ O	075-095	4.12	4.17	Loss of lattice held water molecules
	225-240	4.93	4.98	Loss of coordinated water molecules
	480-520	57.88	57.93	Loss of organic moiety

Table IIS. Kinetics of thermal decomposition studies of La(III) and Th(IV) complexes.

Complex No.	Empirical formula	$\frac{\Delta \log \frac{dw}{dt}}{\Delta \log W_r} \text{ vs } \frac{\Delta T^{-1}}{\Delta \log W_r} \times 10^3 \text{ K}^{-1}$	Order of reaction	Energy of activation E_a (Kcal mol ⁻¹)	
1	La(L ^{II}) ₂ (NO ₃)·2H ₂ O	- 2.75	2.096	0.94	11.10
		- 1.95	1.756		
		- 1.60	1.593		
		- 0.80	1.262		
		0.09	0.914		
		0.96	0.527		
		1.38	0.382		
2	Th(L ^{II}) ₂ (NO ₃) ₂ ·2H ₂ O	1.83	0.186	0.56	20.58
		- 3.802	1.404		
		- 3.411	1.321		
		- 1.672	0.950		
		- 1.480	0.876		
		- 0.580	0.683		
	0.770	0.392			
	1.740	0.164			