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Synthesis, Spectroscopy and Biological Activities of Some Trivalent Lanthanide Complexes of Octadecyl N-salicylaldimine (ONsal)

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A series of Ln(III) complexes of octadecyl N-salicylaldimine (ONsal) were synthesized and characterized by CHN analysis, magnetic moment, conductivity, thermoanalytical and spectroscopic methods. Elemental and thermal analysis data confirmed the formation of heptacoordinated $[Ln(ONsal)_2Cl_2(H_2O)]Cl$ complexes where Ln = Ce^{3+}, Nd^{3+}, Sm^{3+}, Eu^{3+}, Gd^{3+}, Tb^{3+}, Dy^{3+}, Ho^{3+}, which is further supported by the respective mass spectra. The ligand acts as a neutral bidentate species coordinating through azomethine nitrogen and phenolic O-atom. The linkage of one H_2O molecule in all the complexes has been inferred from the thermal analysis. All the Ln(III) complexes are paramagnetic in nature and act as 2:1 electrolyte in 0.002 M DMF at 25 ºC. The complexes of Sm(III), Eu(III) and Tb(III) display luminescent properties. The powder XRD patterns of Nd(III) and Dy(III) complexes could be successfully indexed for monoclinic crystal systems, while the diffraction lines of Eu(III) complex are indexed for a triclinic crystal system. Methanolic solutions of the ligand and complexes were checked for α-glucosidase and α-amylase inhibitory properties where some of the Ln(III) complexes show significant α-glucosidase inhibitory potency while only Tb(III) complex shows inhibition against α-amylase.

Keywords: Lanthanides, Hydrazone, Bidendate, Heptacoordinated, Luminescent, Biological activities.

INTRODUCTION

Coordination chemistry of lanthanides compounds have significantly increased in the last few decades due to their growing use in various chemical and analytical fields, particularly as a fluorescent material and also in medical fields [1-8]. Among the lanthanides, Eu^{3+} and Tb^{3+} ions are particularly useful as substitution probes for spectroscopically silent Ca^{2+} and Mg^{2+} ions in area of allied chemistry [9,10]. The discovery of fluorescence in tryptophan (Trp) with protein parvalbumin codfish binds by Ca^{2+} being quenched by an electron transfer process, when Ca^{2+} binding sites are replaced by Eu^{3+} and Yb^{3+} introduces a new scope in proteins for examining the long-range electron transfer [11]. It has been observed that adding an organic chromophore that forms complexes with the Ln^{3+} ions generally improve the luminescent properties of lanthanides due to favourable energy transfer mechanism of such chromophores to Ln^{3+} ions [12,13]. The N and O donor ligands like hydrazones and their analogs occupy an important place in coordination chemistry. The lanthanide complexes formed by these N and O donor ligands have characteristic properties with a wide spectrum of biological activities and thus are feasible for serving as an ideal system to analyse the functions of biomolecules of the living being [14,15].

The works on the ligation behaviour of several hydrazones towards transition metal and lanthanide ions are also reported in the literature [16-24]. In continuation, we report herein the synthesis and characterization of a series of Ln^{3+} complexes of a hydrazone, octadecyl(N-salicylaldimine)hydrazone (ONsal). Deun & Binnemans [25] reported the synthesis and liquid crystalline properties of ONsal and its complexes with La(III), Nd(III), Gd(III) and Ho(III) nitrates. It has been reported that in the complexes, no mesomorphism could be induced by the ligand. Similarly, the Ln(III) complexes with chlorides as counter ions isolated in this study also do not show any mesogenic properties. The new findings [26-28] about the methylotrophic bacteria which are precisely incorporating the La-Nd into pyrro-loquinolinequinone (PQQ)-dependent

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alcohol dehydrogenases (ADHs) has opened new perspectives of the biological roles of lanthanides. In addition, the omnipresent of lanthanide using organisms and lanthanides binding proteins for selective uptake [29], as a microbial agents and plant growth hormones [30,31] have prompted us to extend our work to the study of the anti-bacterial and antidiabetic properties of the newly synthesized Ln(III) complexes.

EXPERIMENTAL

The materials required for the present study $LnCl_3 \cdot xH_2O$ salts, octadecylamine, α-amylase (from porcine pancreas), starch and 3,5-dinitrosalicylic acid (DNS), purchased from Sigma-Aldrich and salicylaldehyde from Merck, India. Luria Bertani Agar (LBA) and Sabouraud Dextrose Agar (SDA) are obtained from Himedia and α-glucosidase (Maltase, Cat. No. 75551-10) and *p*-nitrophenyl-α-D-glucopyranoside (Cat. No. 12735) from SRL, Mumbai, India. Other reagents were of analytical grade and used as such.

Characterization techniques: Exeter (Model CE-440) CHN-analyzer was used to determine the C, H and N contents. A high temperature muffle furnace (MAC) was used for the metal estimation. In this process, lanthanide(III) complex was heated up to 1000 ºC for 20 h in order to convert them to the corresponding metal oxides. The CON 510 conductivity/TDS meter measured molar conductance at room temperature, wehreas Sherwood's scientific magnetic susceptibility balance measured the magnetic susceptibility with $CuSO_4 \cdot 5H_2O$ as standard reference. TG/DTA data was recorded on an STA-6000 Perkin-Elmer under nitrogen gas heating at a rate of 10 ºC per min. The Shimadzu FT-IR-4800S was used to record the IR-spectra using KBr discs. The electronic absorption spectra were recorded by a Perkin-Elmer UV/visible spectrophotometer, DMSO as solvent with the range of 200-900 nm. The Waters Micromass ZQ 4000 Mass Detector instrument was used to measure the mass spectra. The photoluminescence spectra were recorded on Perkin-Elmer LS-55 fluorescence spectrometer equipped with 20 KW, while the SEM images was recorded on FEI Quanta 250 instrument. The absorbances of α-glucosidase and α-amylase were measured by Thermo-Scientific Multiskan mini spectrophotometer.

Antibacterial assay: The antimicrobial assay of the synthesized lanthanide(III) complexes was carried using the Agar diffusion method [32] with minor modifications. The sterile petri-plates (90 mm) were prepared using 20-25 mL of sterile Luria Bertani Agar and Sabouraud Dextyrose Agar and allowed it to solidify. After approximately 10 min of cleansing, 100 µL of optimized test culture (10^8 CFU/mL) was spread over the solid media to ensure it dried on the plates. Plates with a diameter of 6 mm were produced after solidification by using a sterile coke borer to punch on a well. Two sets, 30 µL and 20 µL, of the test samples, were prepared in DMSO by dissolving 5 mg of each sample in 1 mL and then added separately into the well. The reference antibiotics, gentamycin (10 µg/well) (stock 1 mg/mL) and miconazole (50 mcg/disc) in sterile distilled water were marked as a positive control for the bacteria and fungus, respectively. Then, well with only DMSO solution (30 µL) was utilized as a negative control. The culture plates for bacteria were allowed to incubate at 37 ºC for 24 h and for fungus 25 ºC for 5 days. Once the incubation was completed, the diameter of the inhibition zones developed around the wells was measured in millimeters.An increase in inhibition zones is observed as loading of the complexes increases, suggesting the presence of activity that is dependent on the concentration. The tests were done in triplicate.

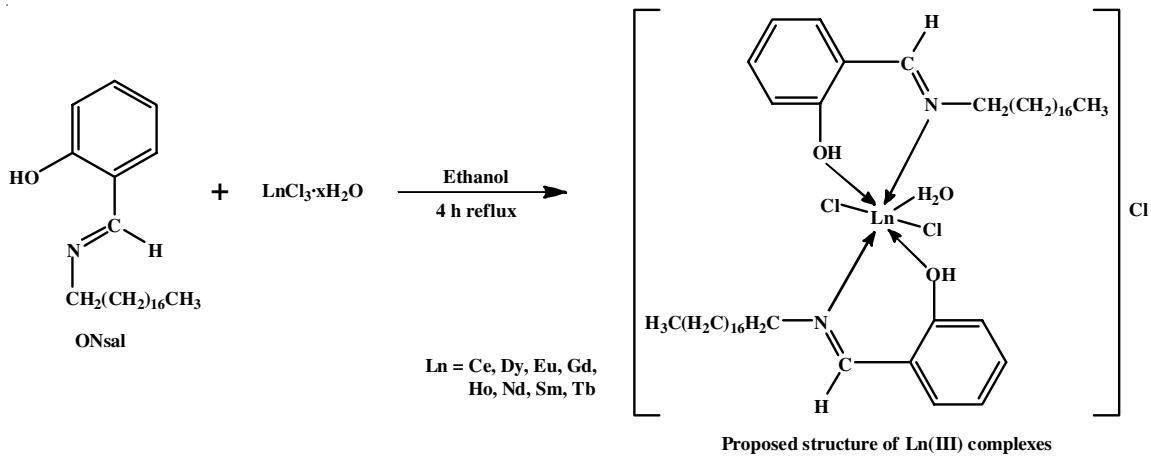
α-Glucosidase inhibitory assay: α-Glucosidase inhibition activities of the ligand (ONsal) and its lanthanide(III) complexes were performed in a 96-well micro-plate according to the reported coulometric method [33]. A spectrophotometer measured the absorbance of colour appearance in the plate with a wavelength of 405 nm. This study used acarbose as a positive reference, DMSO as a negative reference sample with substrate *p*-nitrophenyl-α-D-glucopyranoside (PNPG) as blank. The assay was performed in triplicate with three independent experiments.

α-Amylase inhibitory assay: α-Amylase inhibitory assay was also performed according to the reported colorimetric method [33]. In this study, 0.5% w/v starch solution set in 20 mM phosphate buffer as substrate and DNS colour reagent prepared with (48 mM 3,5-dinitro salicylic acid, 1.063 M sodium potassium tartrate in 2 M NaOH) as reaction stopper of enzyme reaction. Acarbose was used as a positive control (drug) and an uninhibited enzyme was used as a control. The assay was performed in triplicate with three independent experiments.

Synthesis of Ln(III) complexes: Octadecyl(N-salicylaldimine)hydrazone (ONsal) was synthesized as per reported method [25]. In brief, ethanolic solution of ligand (0.5 mmol) was prepared by dissolving 0.180 g in 20 mL absolute ethanol. then an ethanolic solution of cerium(III) chloride (0.25 mmol; 0.093 g in 20 mL absolute ethanol) was added to this solution. After refluxing for 4 h, the reaction mixture was kept in the air for slow evaporation when a light pink Ce(III) complex was obtained (**Scheme-I**). The complex was then separated from the solution by suction, washed with cold ethanol and recrystallized with ethanol. The other Ln(III) complexes were also synthesized in similar manner.

RESULTS AND DISCUSSION

The analytical data of Ln(III) complexes shows that ligand (ONsal) reacted with lanthanide(III) chlorides in ethanolic medium to form stable complexes having the molecular formula, $[Ln(ONsal)_2Cl_2(H_2O)]Cl$ where Ln = Ce, Nd, Sm, Eu, Gd, Tb, Dy, Ho. The complexes are insoluble in water and soluble in hot ethanol, methanol and acetonitrile but readily soluble in coordinating solvents like DMSO and DMF. The stoichiometry of Ln(III) chloride complexes is different from the reported complexes synthesized from the nitrates [25]. In this study, each lanthanide ion is found to be surrounded by two molecules of ligand bonding through the phenolic oxygen and azomethine nitrogen, two chloride ions and one water molecule, giving a seven coordinated species. The physico-chemical data of the complexes are given in Table-1.



Scheme-I: Synthetic route for the Ln(III) complexes

TABLE-1
MELTING POINT, COLOUR, ANALYTICAL DATA, μ_{eff} AND
MOLAR CONDUCTIVITY VALUES OF LIGAND AND Ln(III) COMPLEXES

Ligand/complexes	Decomp. temp. (°C)	Colour	Elemental analysis (%): Found (calcd.)					μ_{eff} (B.M.)		Molar conductance (Ohm^{-1} cm^2 mol^{-1})
			C	H	N	Cl	M	Found	Reported in literature	
ONsal	43	Yellow	80.61 (80.43)	12.05 (11.53)	4.04 (3.75)	–	–	–	–	–
$[Ce(ONsal)_2(H_2O)Cl_2]Cl$	140	Light pink	59.23 (59.29)	8.22 (8.20)	3.09 (2.76)	10.60 (10.52)	14.17 (13.84)	1.92	(2.3-2.5)	107.00
$[Nd(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	120	Dirty brown	58.68 (59.52)	8.18 (8.13)	2.28 (2.78)	10.37 (10.71)	13.53 (14.21)	2.62	(3.5-3.6)	90.00
$[Sm(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	128	Dirty brown	58.64 (58.59)	8.19 (8.11)	2.23 (2.76)	10.42 (10.65)	13.92 (14.73)	0.97	(1.5-1.6)	90.00
$[Eu(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	110	Greenish brown	58.03 (58.43)	8.32 (8.09)	2.30 (2.74)	10.73 (10.62)	14.70 (14.86)	2.96	(3.4-3.6)	93.50
$[Gd(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	133	Dark green	58.03 (58.07)	8.16 (8.05)	2.79 (2.72)	10.42 (10.57)	14.50 (15.30)	7.47	(7.8-8.0)	93.50
$[Tb(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	140	Greenish brown	57.38 (57.97)	8.27 (8.03)	2.25 (2.72)	10.55 (10.53)	16.03 (15.44)	8.02	(9.4-9.6)	98.50
$[Dy(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	142	Dirty brown	57.57 (57.91)	7.56 (7.98)	2.73 (2.71)	11.34 (10.51)	15.07 (15.73)	9.19	(10.4-10.5)	97.50
$[Ho(ONsal)_2(H_2O)Cl_2]Cl·H_2O$	130	Dark green	57.35 (57.80)	7.88 (7.90)	2.85 (2.70)	10.19 (10.49)	16.12 (15.93)	9.38	(10.3-10.5)	103.00

All the lanthanide(III) complexes are paramagnetic, however, the magnetic moment values are slightly lower than the reported values [34], suggesting a possible antiferromagnetic coupling interaction between the metal centers in the crystal lattice. The molar conductivity values indicate 2:1 electrolytic nature of complexes in 0.002 M DMF at 25 ºC [34].

Mass spectral studies: Despite numerous efforts, single crystals could not be obtained. Therefore, to authenticate the molecular formulae of the Ln(III) complexes proposed on the basis of elemental data and thermal studies, we recorded the mass spectra of the lanthanide(III) complexes which are given in Fig. 1. The strong peaks at *m/z* 270 and 374 detected correspond to the molar mass of octadecylamine and the ligand fragments, respectively. The peak at *m/z* 1012-1036 confirmed the formation of complexes having a 1:2 metal ligand molar ratio with the molecular formula $[Ln(ONsal)_2Cl_2(H_2O)]Cl$. The proposed structures and the molecular weights of lanthanide(III) complexes are included in the respective spectra.

IR spectral studies: The IR spectral data of ligand and its lanthanide(III) complexes are summarized in Table-2. The band at 1633 cm^{-1} due to ν(C=N) in the ligand spectrum shows a hypsochromic shift in the spectra of complexes indicating involvement of azomethine nitrogen in coordination [35]. Bonding of the phenolic oxygen to the metal ions is inferred from the observed hypsochromic shift of the $\nu(C_{ph}\text{-}O)$ in the spectra of the Ln(III) complexes [36]. The bands at lower frequency regions 460-450 and 420-410 cm^{-1} in the spectra of the complexes may be attributed to ν(Ln-O) and ν(Ln-N) modes, respectively which further supports the ligand to metal bonding [37].

Electronic spectral studies: The electronic absorption spectra of ligand ONsal and its Ln(III) complexes recorded in DMSO solution at room temperature are shown in Fig. 2. The spectrum of the ligand exhibits two strong peaks, one at 264 due to the π→π* transition of the aromatic ring of the ligand [38,39] and another at 314 nm corresponding to the π→π*

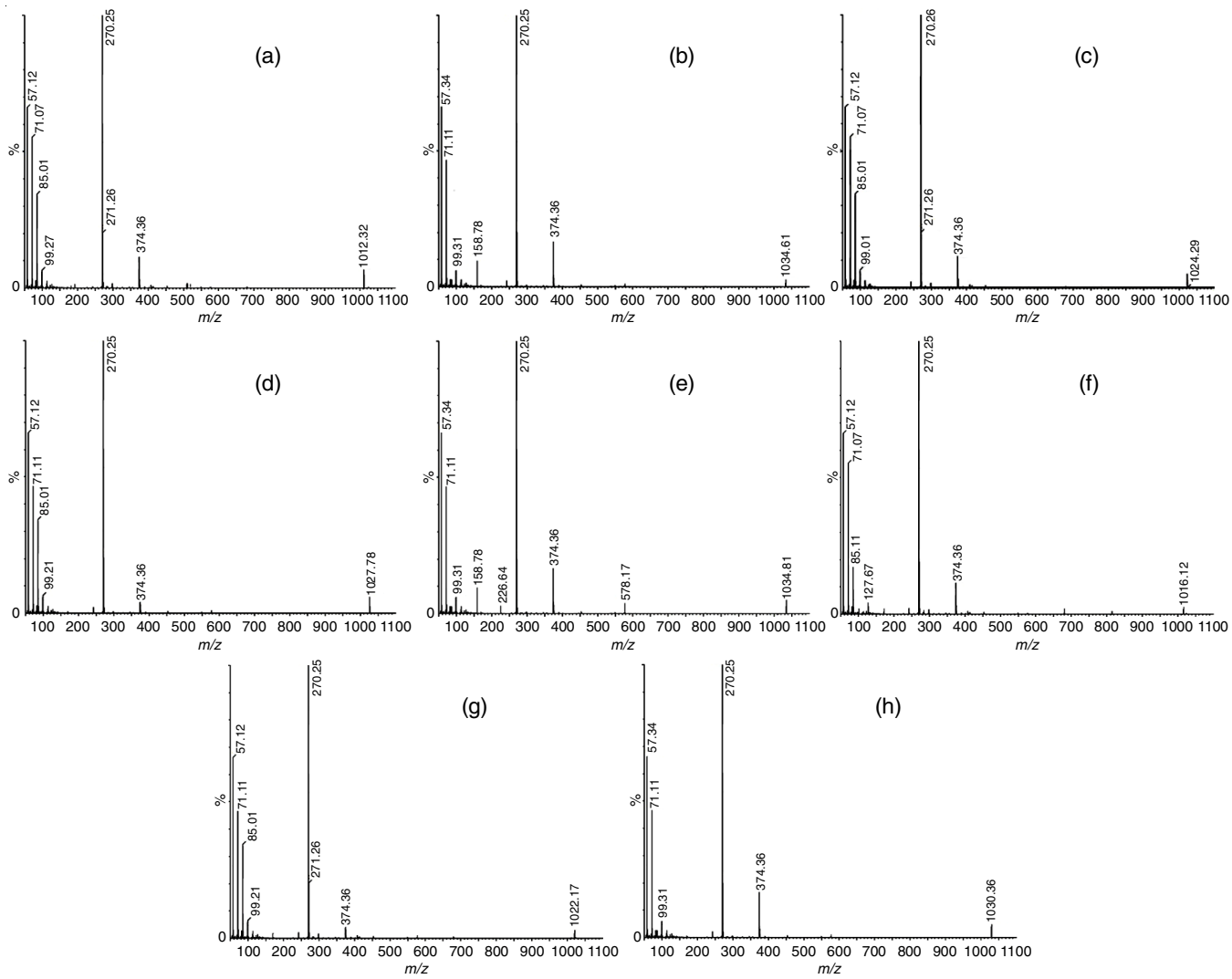


Fig. 1. Mass spectrum of (a) $[Ce(ONsal)_2Cl_2(H_2O)]Cl$, (b) $[Dy(ONsal)_2(H_2O)Cl_2]Cl$, (c) $[Eu(ONsal)_2(H_2O)Cl_2]Cl$, (d) $[Gd(ONsal)_2(H_2O)Cl_2]Cl$, (e) $[Ho(ONsal)_2(H_2O)Cl_2]Cl$, (f) $[Nd(ONsal)_2(H_2O)Cl_2]Cl$, (g) $[Sm(ONsal)_2(H_2O)Cl_2]Cl$ and (h) $[Tb(ONsal)_2(H_2O)Cl_2]Cl$

TABLE-2
IR SPECTRAL DATA (cm^{-1}) OF ONsal AND Ln(III) COMPLEXES AND THEIR ASSIGNMENTS

Ligand/ complexes	ν(O-H)	ν(C-H)	ν(C=N)	ν(C=C)	ν(CH_2)	ν(C-N)	ν(C_{ph}-O)	ν(Ln-O)	ν(Ln-N)
Onsal	–	2918, 2848	1633	1579	1468	1336	1248	–	–
Ce(III)	3832	2925, 2855	1659	1607	1469	1373	1293	458	415
Nd(III)	3832	2916, 2847	1658	1606	1469	1348	1292	458	415
Sm(III)	3831	2916, 2848	1658	1606	1469	1348	1292	457	415
Eu(III)	3832	2916, 2848	1658	1606	1469	1375	1292	459	414
Gd(III)	3828	2916, 2848	1658	1606	1469	1371	1292	459	417
Tb(III)	3832	2918, 2848	1653	1589	1469	1373	1305	458	413
Dy(III)	3832	2916, 2848	1656	1593	1469	1373	1305	457	419
Ho(III)	3832	2922, 2848	1658	1595	1469	1370	1305	457	416

transition involving the molecular orbitals centered on the azomethine-N and the benzene ring [40]. A decrease in the intensity of these bands in the spectra of Ln(III) complexes is suggestive of the participation of the azomethine nitrogen in complexation. The spectra of the complexes in fact appeared as a simple blending arising from the spectra of free ligand and $LnCl_3 \cdot xH_2O$.

Photoluminescence studies: The emission spectra recorded in DMSO solution at λ_{ex} = 362 nm are shown in Fig. 3. A broad fluorescence band at 438 nm attributable to $\pi \rightarrow \pi^*$ transition observed in the emission spectrum of the ligand undergoes a blue shift in the spectra of Ln(III) complexes inferring that these electrons are taking part in complexation [41,42]. Among the complexes under study, Eu(III), Sm(III) and Tb(III) comp-

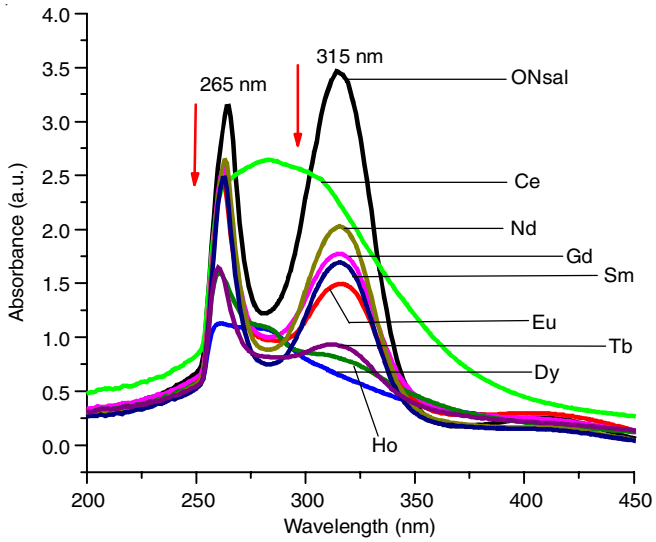


Fig. 2. Electronic absorption spectra of the ligand and the complexes

lexes exhibit the characteristic emission bands at room temperature, indicating fulfillment of one or all the conditions required for Ln(III) complexes to be highly luminescent [43,44]. The emission spectrum of Tb(III) displays four luminescence bands at 491, 546, 584 and 618 nm owing to the transitions $^5D_4 \rightarrow {}^7F_6$, $^5D_4 \rightarrow {}^7F_5$, $^5D_4 \rightarrow {}^7F_4$ and $^5D_4 \rightarrow {}^7F_3$, respectively. The bands due to transitions $^5D_4 \rightarrow {}^7F_5$ and $^5D_4 \rightarrow {}^7F_6$ strongly exhibit green and blue emission, respectively [45]. For Sm(III) complex, the spectrum displays three luminescence bands at 565 nm due to $^4G_{5/2} \rightarrow {}^6H_{5/2}$, 602 nm for $^4G_{5/2} \rightarrow {}^6H_{7/2}$ and 647 nm due to $^4G_{5/2} \rightarrow {}^6H_{9/2}$ transitions. The Eu(III) emission bands are observed at 595, 618 and 703 nm matching with $^5D_0 \rightarrow {}^7F_1$, $^5D_0 \rightarrow {}^7F_2$ and $^5D_0 \rightarrow {}^7F_4$ transitions, respectively. These results showed the efficient chelating ability of the ligand enabling it to transfer energy to the metal ions.

Thermogravimetric studies: The thermogravimetric decomposition of the Ln(III) complexes was recorded in the temperature range 30-800 ºC in an inert nitrogen atmosphere

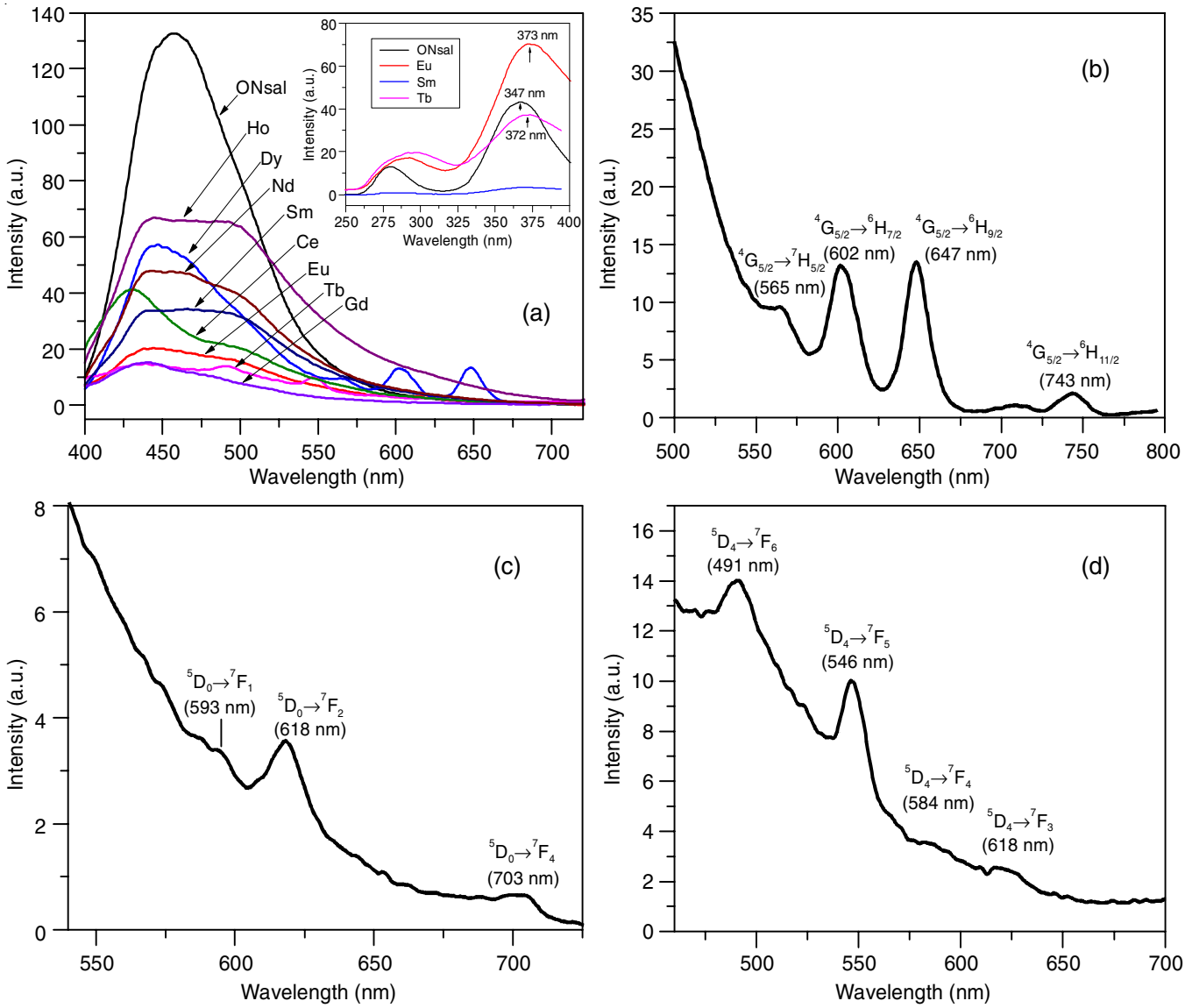


Fig. 3. Fluorescence spectra (λ_{ex} = 362 nm), (a) Spectra of ONsal and Ln(III) complexes; Inset, Excitation spectra of ONsal, Eu(III), Sm(III) and Tb(III) complexes. Enlarged spectra of (b) Sm(III), (c) Eu(III) and (d) Tb(III) complexes

at the heating rate of 10 ºC/min and the analysis data is given in Table-3.

The thermal decomposition reaction of Ln(III) complexes would proceed through three stages *viz*. dehydration, loss of three chloride ions and decomposition of ligand moiety resulting in the formation of the corresponding Ln(III) oxide. The thermogram of Ce(III) complex is shown in Fig. 4 as a representative one. The thermogram indicates dehydration for the water molecule in the temperature ranging between 147 to 201 ºC. During the dehydration of $[Ce(ONsal)_2(H_2O)Cl_2]\cdot Cl$ to $[Ce(ONsal)_2Cl_2]\cdot Cl$, the experimental mass loss value of 2.10% is in good agreement with the theoretical mass loss value of 1.78%. Loss of the three chloride ions and the two ligand molecules from $[Ce(ONsal)_2Cl_2]\cdot Cl$ to form Ce_2O_3 occurs continuously from 201 to 607 ºC. In this stage, there are two mass losses in between 201 and 600 ºC, the rapid mass loss to 367 ºC followed by a slower mass loss to 607 ºC. The experimental mass loss value of 83.93% is at par with the theoretical value of 84.38% for the decomposition stages of $[Ce(ONsal)_2Cl_2]\cdot Cl$ to Ce_2O_3. The final residue that remains at 607 ºC from the thermal decomposition is the corresponding metal(III) oxide. The results are almost identical to each other and the thermograms of the remaining complexes exhibit the similar features.

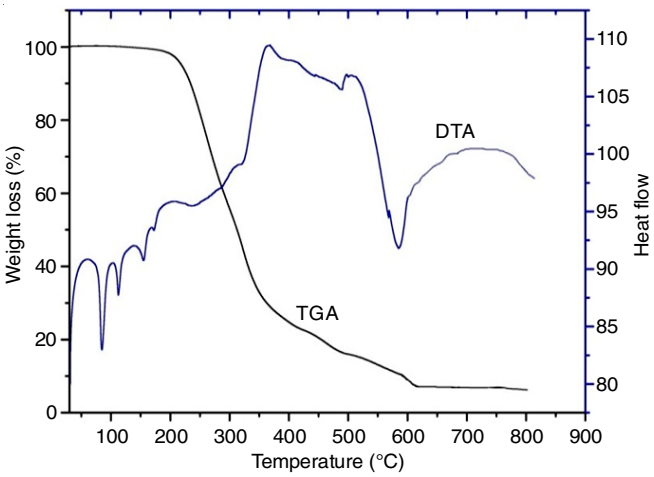


Fig. 4. TG/DTA curve of $[Ce(ONsal)_2(H_2O)Cl_2]Cl$

Powder XRD studies: The diffraction pattern of ligand ONsal and its Ln(III) complexes was examined in the range 10-70º at 1.3923 Å and the diffraction lines of only Nd(III), Eu(III) and Dy(III) complexes could be successfully indexed [46]. The XRD patterns of Nd(III) and Dy(III) complexes indexed for the monoclinic crystal systems yield the lattice constants, a = 14.4619 Å, b = 5.9042 Å, c = 9.0925 Å and unit cell volume V = 651.71 $Å^3$ for Nd(III) and a = 20.5118 Å, b = 7.8318 Å, c = 16.8584 Å and unit cell volume V = 1426.55 $Å^3$ for Dy(III) complex. However, the diffraction lines of Eu(III) complex was indexed for a triclinic crystal system giving the lattice parameters, a = 7.2322 Å, b = 6.0275 Å, c = 11.4827 Å and V = 491.82 $Å^3$.

Antimicrobial activities: Ligand ONsal and its Ln(III) complexes were examined for antibacterial activity against four bacteria, two strain of Gram-negative *viz. Escherichia coli* ATCC-11632 and *Pseudomonas aeruginosa* ATCC-15442 and two strains of Gram-positive *viz. Staphylococcus aureus* ATCC-11632 and *Bacillus cereus* MTCC-430. The antifungal activities were examined against two species of fungus *viz. Microsporum fulvum* MTCC-2837 and *Trichophyton metagrophyte* MTCC-8687.

The minimum inhibition concentration (MIC) of compound and reference antibiotic (gentamycin) was determined as follows: In brief, the test sample was dissolved in 10% (v/v) DMSO/MHB to give a final concentration of 500 µg/mL. This was further serially diluted two-fold to obtain concentration ranges of 0.425-50 µg/mL and the standard was found in the concentration range of 0.156-10 µg/mL. A 100 µL of each concentration was added in a well (96-well microplate) containing 100 µL of inoculum. An inoculum density of 1×10^6 CFU/mL of bacterial strains was prepared as prescribed [47]. DMSO in the well was less than 3% in the final concentration. The negative control well comprised of 100 µL of MHB and 100 µL of the standard inoculum [48]. Using sterile plate sealer, the plates were covered and agitated to mix the contents of the wells using a plate shaker and incubated at 37 ºC for 24 h. The experiment was repeated three times. The MIC of ligand ONsal and its Ln(III) complexes was detected following additional addition (40 µL) of 0.2 mg/mL nitroblue tetrazolium chloride (NBT) to microplates wells and incubated at 37 ºC for 30 min [49].

TABLE-3
TG/DTA DATA OF Ln(III) COMPLEXES

Complexes	Temperature range (°C)	Weight lost (%)	Decomposition part
Ce	157-201	2.10 (1.76)	One coordinated water molecule
	201-607	83.93 (84.38)	Three chloride ions and two ligand molecules
Nd	148-191	2.36 (1.78)	One coordinated water molecule
	191-590	73.52 (84.10)	Three chloride ions and two ligand molecules
Sm	153-199	2.14 (1.76)	One coordinated water molecule
	199-510	83.12 (83.53)	Three chloride ions and two ligand molecules
Eu	160-196	2.04 (1.76)	One coordinated water molecule
	196-610	82.81 (83.52)	Three chloride ions and two ligand molecules
Gd	163-200	2.15 (1.75)	One coordinated water molecule
	200-684	82.78 (83.47)	Three chloride ions and two ligand molecules
Tb	147-205	2.24 (1.75)	One coordinated water molecule
	205-595	82.72 (83.45)	Three chloride ions and two ligand molecules
Dy	160-220	2.04 (1.74)	One coordinated water molecule
	220-586	82.16 (83.22)	Three chloride ions and two ligand molecules
Ho	154-210	2.10 (1.75)	One coordinated water molecule
	210-572	82.08 (83.05)	Three chloride ions and two ligand molecules

TABLE-4
ANTIMICROBIAL ACTIVITIES OF THE LIGAND AND ITS Ln(III) COMPLEXES ('–', inactive)

Ligand/ complexes	Concentration (µg/mL)	Diameter of zone of inhibition (mm)/Each well = 6 mm					
		Gram-negative bacteria		Gram-positive bacteria		Fungus	
		Pseudomonas aeruginosa	*Escherichia coli*	*Bacillus cereus*	*Staphylococcus aureus*	*Microsporum fulvum*	*Trichophyton metagrophyte*
ONsal	150	10	–	14	11	–	–
	100	9	–	12	9	–	–
Ce	150	–	–	12	10	–	–
	100	–	–	10	8	–	–
Nd	150	–	–	–	–	–	–
	100	–	–	–	–	–	–
Sm	150	–	–	10	13	–	–
	100	–	–	8	12	–	–
Eu	150	10	–	14	13	–	–
	100	8	–	12	12	–	–
Gd	150	12	–	13	13	–	–
	100	10	–	11	10	–	–
Tb	150	–	–	10	12	–	–
	100	–	–	8	11	–	–
Dy	150	–	–	13	13	–	–
	100	–	–	11	11	–	–
Ho	150	–	–	11	10	–	–
	100	–	–	9	8	–	–
Gentamycin (10 µg/well)		18	20	22	20	-	–
Micronazole (50 mcg/disc)		–	–	–	–	16	18
DMSO (negative control) 30 µL		–	–	–	–	–	–

As shown by Table-4, all the Ln(III) complexes display the antimicrobial activity against some strains higher than the ligand. The Ln(III) complexes except for Nd(III) complex exhibit fairly high activities against the Gram-positive *Bacillus cereus* and *Staphylococcus aureus* compared to the ligand. However, the complexes show activity against the Gram-negative bacteria (*E. coli*) while Eu(III) and Gd(III) complexes no activity against *P. aeruginosa*. The inactivity stems found from the higher lipid content in the cell membrane of *P. aeruginosa* and *E. coli* compared to *B. cereus* and *P. aeruginosa* prevent diffusion of the Ln(III) complexes into the cell. Increase in the activities of the complexes over the ligand against Gram-positive bacteria is ascribed to the synergistic effect which increases the lipophilicity of complexes [50]. An increase in the lipophilicity of the complexes permits easy penetration into the lipid membranes of organisms, facilitating blockage of metal-binding sites in enzymes. It is observed from Table-5 that the inhibition by Ln(III) metal chelation is greater than that of ligand, due to the lipophilic character of the lanthanide(III) ions in complexes [51]. The enhance in activities with loading account for the effect of metal ions during the process.

The enhancement of activity on chelation is accredited to the electron delocalization over the metal and donor atoms of ligand, increasing the lipophilic nature of the metal chelate and easier infusion to the bacterial membranes *via* lipid layers. Further, enhanced biological activities of the metal complexes in comparison to the ligand also depends on conductivity, dipole moment and solubility with the presence of metal ions.

Antidiabetic activities: Ligand ONsal and its Ln(III) complexes were also investigated for α-glucosidase and α-amylase activities and the results are shown in Table-6. As observed, only Ce(III), Nd(III), Gd(III) and Tb(III) complexes show significant α-glucosidase inhibitory activities, the order of which is Tb > Ce > Gd > Nd, werheas moderate α-amylase inhibition activity is observed only for Tb(III) complex.

TABLE-5
MIC (µg/mL) OF THE LIGAND/Ln(III) COMPLEXES ('–': inactive)

Ligand/ complexes	Gram-negative bacteria	Gram-positive bacteria	
	Pseudomonas aeruginosa	*Bacillus cereus*	*Staphylococcus aureus*
ONSal	50	12.5	25.0
Ce	–	25.0	50.0
Sm	–	12.5	12.5
Eu	50	12.5	12.5
Gd	25	12.5	25.0
Tb	–	25.0	25.0
Dy	–	12.5	12.5
Ho	25	12.5	12.5
Gentamycin (µg/mL)	5	5	5

TABLE-6
HALF MAXIMUM INHIBITORY CONCENTRATION (IC_{50}) OF THE TESTED SAMPLES ON THE α-GLUCOSIDASE AND α-AMYLASE. ACTIVITIES OF THE STANDARD SAMPLE

Ln(III) complexes	α-Glucosidase (IC_{50})	α-Amylase (IC_{50})
Ce	181.078 ± 1.20	–
Gd	187.60 ± 3.92	–
Nd	191.65 ± 2.12	–
Tb	127.24 ± 1.26	149.29 ± 0.56
Acarbose	331.71 ± 10.46	8.96 ± 0.40

Conclusion

Lanthanide(III) complexes of octadecyl N-salicylaldimine (ONsal) of the type $[Ln(ONsal)_2Cl_2 \cdot H_2O] \cdot Cl$, where Ln = Ce, Nd, Sm, Eu, Gd, Tb, Tb, Ho were synthesized and characterized. The conductivity measurement showed that all lanthanide(III) complexes behave as 2:1 electrolyte in 0.002 M DMF at 25 ºC. The FT-IR spectral data confirmed the coordination of the ligand as a neutral bidentate species through the azomethine nitrogen and phenolic oxygen. Fluorescent spectroscopic investigation shows that ligand optimizes the luminescent properties of the Ln(III) ions and energy transfer occurs between the ligand and the Ln(III) ions. Antimicrobial studies suggested that the ligand and synthesized Ln(III) complexes exhibit good antibacterial activity against the tested bacteria. The Ce(III), Nd(III), Gd(III) and Tb(III) complexes exhibit significant α-glucosidase inhibitory activity while moderate α-amylase inhibition potency is observed only for Tb(III) complex.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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