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Synthesis and Spectral Studies of Piprazine Schiff Base Lanthanide(III) Complexes and their Microbial and Anticancer Activity

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A novel Schiff base ligand has been synthesized by the condensation reaction of 1-(2-amino ethyl)piprazine with *o*-vanillin in methanol solution. Using lanthanide(III) metal ions (Ln^{3+} = La^{3+}, Ce^{3+}, Pr^{3+}, Nd^{3+}, Sm^{3+} and Gd^{3+}) in methanol, six complexes of piprazine Schiff base were synthesized. All the lanthanide(III) complexes were characterized by IR, UV, NMR, TG-DTA, X-ray diffraction analysis and photoluminence. According to the spectral analysis piprazine act as a bidentate monobasic donor coordinating through the azomethine nitrogen and a phenyl oxygen atom. Antimicrobial studies of the synthesized compounds were evaluated and reported. Anticancer activities were also studied towards the human breast cancer cell line (MCF-7).

Keywords: Schiff base, lanthanide(III) complexes, Antimicrobial activity, Anticancer activity.

INTRODUCTION

The globally upgrade change needs to establish a relegate synthetic assessment for synthetically and biologically important compounds. Lanthanide(III) metal complexes and their Schiff base ligand have been exposed to illustrate a variety of applications including biological, clinical, analytical and industrial in addition to their important roles in catalysis and organic synthesis [1-3]. The coordination chemistry of lanthanides and their complexes have aroused more significance in Schiff base can coordinate to many lanthanide ions [3]. Therefore, an experiment has been made to synthesize, characterization and biological activity of some lanthanide(III) Schiff base complexes containing N, O donor atoms.

The piperazine and its derivatives are more interesting ligands due to their great bridging ability. Usually, they are employed to form building blocks in coordination polymers [4-9]. Piperazine moiety has much biologically active compounds introducing the antimicrobial [10] and related quinolines, dopaminergic D3 agents [11], HIV protease inhibitors(II) acid and the antidepressant [12]. Piperazine derivatives were pervasively explored and used as drugs in the field of medical sciences and actively probed in antibacterial, antifungal and anticancer aspects [13-25].

EXPERIMENTAL

Synthesis of 2-methoxy-6-((2-(piperazin-1-yl)ethylimino)methyl)phenol ligand (L2): To synthesize unsymmetrical tetradentate Schiff base ligand (L_2) was condensed by 1-(2-aminoethyl)piperazine (0.001 mol, 0.1312 mL) with *o*-vanillin (0.001 mol, 0.152 g) mixed in 1:1 mmol ratio under boiling on a water bath at 50 ºC for 4-5 h. The Schiff base solution was turned to yellow colour.

Synthesis of lanthanide(III) nitrate: By the conversion of lanthanide(III) metal oxides such as La_2O_3, CeO_2, Pr_6O_{11}, Nd_2O_3, Sm_2O_3 and Gd_2O_3 to lanthanide(III) nitrate salts by dissolving 1:1 ratio with the conc. HNO_3 acid and remove the excess of acid by evaporation. The final residues were dissolved in 20 mL of methanol and ether was used for the synthesis of metal complexes.

Synthesis of Ln(III) metal complexes: All the lanthanide complexes *viz.* La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) were synthesized by *in situ* method. The Schiff base solution (L_2) (1 mmol) and methanolic solution of Ln(III)

nitrate (1 mmol) was added slowly in dropwise, mixed well and boiled on a water bath at 50 ºC for 4-5 h. The precipitate were obtained, filtered off and dried in air. All the complexes with good yields, were stable in air, non-hygroscopic and decomposed above 270 ºC. These complexes were soluble in DMF and DMSO whereas insoluble in other organic solvents.

Antimicrobial activity: The antibacterial activity of Schiff base and its Ln(III) complexes were evaluated against two Gram-positive (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative bacteria (*Escherichia coli* and *Pseudomonas auroginosa*) using disc diffusion method and compared with standard drug ciprofloxacin. The antifungal activity was evaluated against two species namely *Candida albicans* and *Aspergillus niger* and compared with the standard drug clotrimazole.

Anticancer activity: The *in vitro* anticancer activity of Schiff base ligand (L_2) and its Ln(III) complexes were also evaluated against human breast cancer cell lines (MCF7) with the concentration ranges (6.25, 12.5, 25, 50 and 100 µg/mL) and using a colorimetric MTT assay.

RESULTS AND DISCUSSION

Molar conductivity measurements: At room temperature, the molar conductivity of Ln(III)-piperazine based Schiff base complexes ($Ln(NO_3)_3(CH_2O)L_2$) were evaluated in the DMSO solvent. The molar conductivity values in the range of 110-123 ohm^{-1} cm^2 mol^{-1} showed that the all the complexes are in 1:1 electrolytic nature. The physical and analytical data of the synthesized Ln(III) complexes are given in Table-1.

FT-IR spectra: The FT-IR spectra of the Schiff base (L_2) and its Ln(III) complexes were done in the range of 4000-400 cm^{-1}. The free ligand (L_2) shows – C=N band at 1689 cm^{-1} moved to lower frequencies in all the six Ln(III) complexes, which demonstrated that azomethine nitrogen facilitated to the metal site. Ligand (L_2) shows phenolic –OH and –NH stretching vibrations showed up as envelopes in the region of 3317-3302 cm^{-1}. The disappearing of –OH stretching band in the complexes is because of the deprotonation of coordination to Ln(III) ions [8]. In the complexes, –NH extending vibrations was converged with –OH extending of the planned water molecule (νH_2O) in 3155-3047 cm^{-1} revealed that the optional nitrogen of piperazine ring associated with the coordination.

In the lanthanide(III) complexes, –OH stretching broad band of the coordinated water molecule appeared at 3441-3404 cm^{-1}. The vibrations of the methoxy group appeared at 2900-2839 cm^{-1} in stretching mode. All the Ln(III) complexes have a strong band at 1381 cm^{-1} specifying the presence of ionic nitrate. The coordinated water molecule of rocking mode appe-ared at 825.53 cm^{-1}. Also, the magnitude of (ν_4-ν_1) and (ν_3-ν_5) were about 147-177 cm^{-1} and 54-59 cm^{-1}, signifying that the nitrate ion involved in the coordination in bidentate nature. The new ν(Ln-O) and ν(Ln-N) bands performed in the region 438-426 and 586-564 cm^{-1}, respectively (Table-2).

Electronic spectra: The electronic spectra of Pr(III), Nd(III) and Sm(III) with ligand (L_2) and its complexes were studied and related with the spectra of the resultant aqua ions are shown in Fig. 1a-d. The n-π* and π-π* transition at 350 and 304 nm shows for Schiff base ligand (L_2). In the complexes,

TABLE-1
PHYSICAL AND ANALYTICAL DATA OF Ln(III) COMPLEXES OF SCHIFF BASE LIGAND (L_2)

Complexes	m.w.	Yield (%)	m.p. (°C)	Elemental analysis (%): Observed (calcd.)					Conductance (ohm^{-1} cm^2 mol^{-1})
				L_2	M	C	H	N	
$La(NO_3)_2(H_2O)_2L_2$	561.28	70	210	46.65 (45.74)	24.66 (24.84)	30.13 (30.07)	3.59 (3.54)	8.22 (8.02)	115.7
$Ce(NO_3)_2(H_2O)_2L_2$	562.49	75	180	46.65 (45.74)	25.08 (25.00)	30.08 (30.00)	3.58 (3.52)	7.18 (7.49)	122.5
$Pr(NO_3)_2(H_2O)_2L_2$	563.28	78	225	46.65 (45.74)	25.11 (26.60)	29.96 (30.70)	3.58 (3.54)	7.49 (7.53)	110.2
$Nd(NO_3)_2(H_2O)_2L_2$	566.61	77	200	46.65 (45.74)	25.55 (24.64)	29.78 (29.96)	3.56 (3.55)	7.44 (7.50)	117.5
$Sm(NO_3)_2(H_2O)_2L_2$	572.73	65	210	46.65 (45.74)	26.22 (26.35)	29.52 (29.46)	3.52 (3.54)	7.42 (7.36)	123.3
$Gd(NO_3)_2(H_2O)_2L_2$	579.62	70	217	46.65 (45.74)	27.24 (27.22)	29.07 (29.11)	3.48 (3.42)	7.29 (7.27)	114.6

TABLE-2
FT-IR DATA (cm^{-1}) OF LIGAND (L_2) AND ITS Ln(III) NITRATE COMPLEXES

Compd.	ν(O-H)	ν(H_2O)	ν(C=N)	ν(N-H)	ν(NO_3)	Ionic nitrate	ν(Ln-O)	ν(Ln-N)	ν_4	ν_1	ν_2	ν_6	ν_3	ν_5	ν_4–ν_4	ν_3–ν_5
L_2	3302	–	1689	3317	–	–	–	–	–	–	–	–	–	–	–	–
La^{3+}	–	3394	1658	–	1327	1381	430	578	1504	1327	1018	825	779	725	177	54
Ce^{3+}	–	3404	1658	–	1327	1381	426	564	1504	1327	1018	825	779	725	177	54
Pr^{3+}	–	3425	1658	–	1357	1381	438	578	1504	1357	1010	825	780	725	147	55
Nd^{3+}	–	3433	1650	–	1357	1381	430	586	1504	1357	1018	825	780	725	147	55
Sm^{3+}	–	3425	1658	–	1327	1381	426	586	1504	1327	1018	825	782	725	177	57
Gd^{3+}	–	3441	1658	–	1327	1381	438	586	1504	1357	1018	825	784	725	123	59

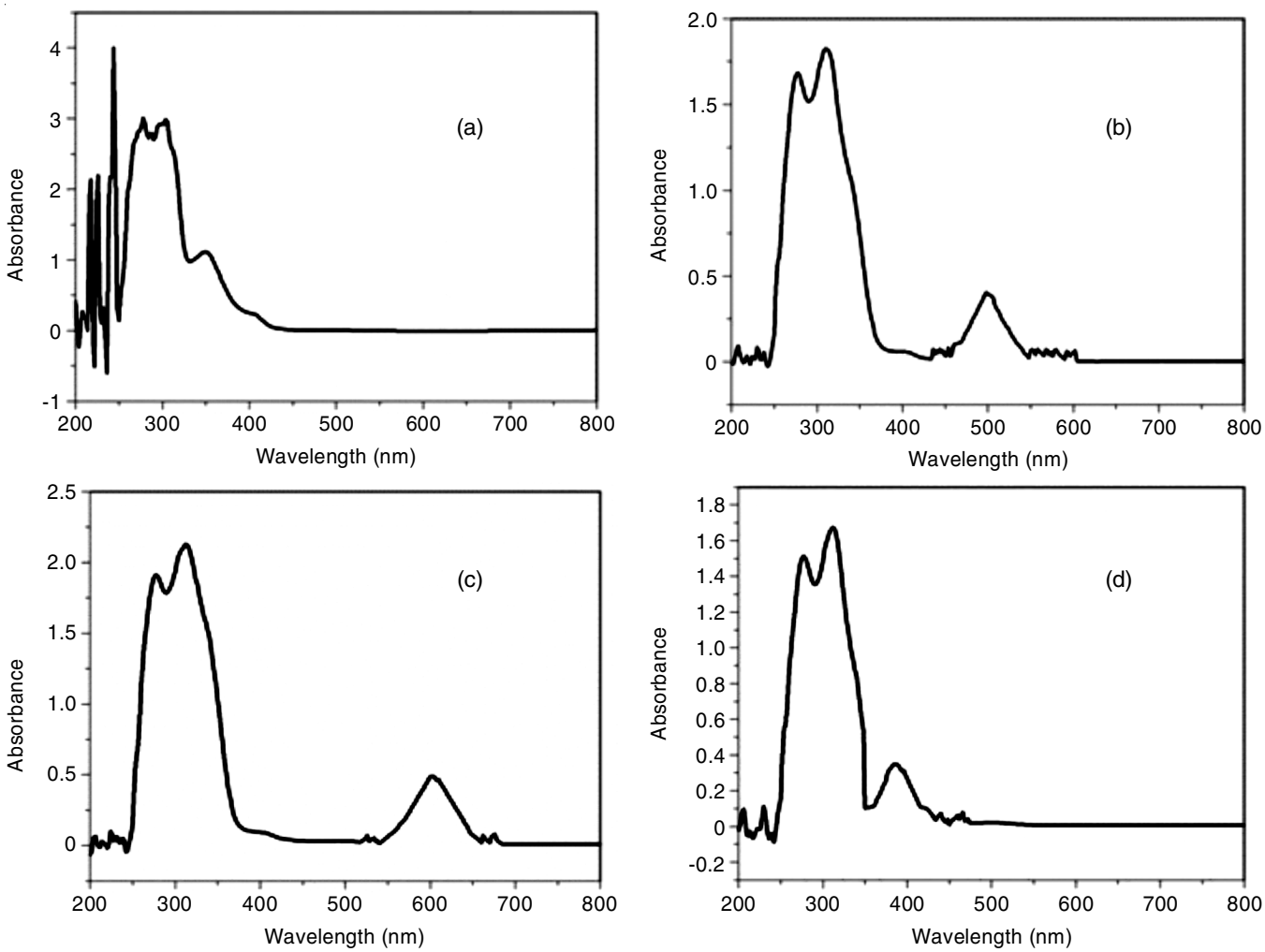

Fig. 1. UV-visible spectrum of (a) 3-methoxy-2-((2-piperazin-1-yl)ethylimino)methyl)phenol (L_2); (b) praseodymium(III) complex; (c) neodymium(III) complex; (d) samarium(III) complex

these bands appear at n-π* 312 nm and π-π* 278 nm. The electronic spectra of the complexes show redshift and also a transformation in the intensity, compared to those of the aqua ions [14]. The visible spectral bands are hypersensitive for the lanthanide complexes due to *f-f* transitions being very weak. The red shift leads to the measure of the covalent nature of metal-ligand interaction by bonding parameter ($\beta^{1/2}$) and the covalency angular overlap parameter (η). The Pr(III) complex shows three transitions $^3H_4 \rightarrow {}^1D_2$, $^3P_0$ and $^3P_2$. The absorption band linked with $^3H_4 \rightarrow {}^1D_2$ exhibited strong hypersensitive behaviour. The spectral profiles of the Nd^{3+} complex show three transitions with three bands $^4I_{9/2} \rightarrow {}^4G_{7/2}$, $^2G_{7/2}$ and $^4G_{5/2}$ (hypersensitive band). The Sm(III) complex indicates three transition band at $^4H_{5/2} \rightarrow {}^4F_{9/2}$, $^6P_{5/2}$ and $^4I_{5/2}$. The β values for these complexes are starting to be less than unity. The values of $\beta^{1/2}$ and $\delta > 1$ were found to be positive, which indicated the covalency in the metal-ligand bonding (Table-3).

NMR studies: The ^1H & ^{13}C NMR spectra were recorded in DMSO-d_6 solvent for piperazine based Schiff base ligand (L_2) and its Ln(III) complexes [LaL_2, CeL_2, PrL_2 and NdL_2]. The azomethine proton of the piperazine based Schiff base ligand (L_2) displays a singlet peak at 8.14 ppm. The phenolic proton of the free ligand appeared at 9.51 ppm. The NH proton of the piperazine ligand ring appeared as singlet broad band in the region of 2.4 ppm. The H(2′) and (3′) protons at 2.55 ppm and H(4′) proton appeared as triplet at 2.71 ppm of the piperazine ring. The singlet peak at 3.79 ppm is due to three protons of the methoxy group of *o*-vanillin. The aromatic protons are resonated as multiplet in the region of 7.00-7.33 ppm. The coordinated water proton and azomethine proton of the complexes appeared at 9.5-12.7 ppm and 8.25 to 8.29 ppm. The disappearance of phenolic proton peaks in all the complexes indicating deprotonation and consecutive to the metal sites [15]. The NH protons of the piperazine ring with higher intensity than the free ligand show secondary nitrogen atom involved in the coordination showed at 2.42-2.50 ppm. In the complexes, the methoxy group of *o*-vanillin moiety appeared as singlet in the range of 3.76-3.79 ppm. The azomethine carbon appeared at 162.10 ppm for the piperazine based Schiff base ligand (L_2). In Ln(III) complexes, the coordination to azomethine nitrogen shows a peak at downfield shift. The aromatic ring carbon atoms appeared at 123.47, 127.54, 148.39 and 150.58 ppm in Schiff base ligand and their Ln(III) complexes. The aliphatic carbon atom showed at 26.04, 34.33, 42.06, 45.42, 46.74,

TABLE-3
UV-VISIBLE DATA OF LIGAND (L_2) AND ITS Ln(III) NITRATE COMPLEXES

Complex	Magnetic moment (B.M.)	Ln aquo complexes (cm^{-1})	Ln(III) complexes (cm^{-1})	Energy levels	(1-β)	β	$\beta^{1/2}$	δ%	H
Pr^{3+}	1.7	22497	21930*	$^3H_4 \rightarrow {}^1D_2$	0.02520	0.97480	0.15876	2.58515	0.01252
		21322	20980	$^3H_4 \rightarrow {}^3P_0$	0.01604	0.98396	0.12665	1.63015	0.00799
		20738	20557	$^3H_4 \rightarrow {}^3P_2$	0.00873	0.99127	0.09343	0.88069	0.00218
Nd^{3+}	2.9	28249	27552	$^4I_{9/2} \rightarrow {}^4G_{7/2}$	0.02468	0.97532	0.15709	2.53045	0.01226
		19164	18730	$^4I_{9/2} \rightarrow {}^4G_{5/2}$	0.02265	0.97735	0.15050	2.31749	0.01126
		17406	17182*	$^4I_{9/2} \rightarrow {}^2G_{7/2}$	0.01287	0.98713	0.11345	1.30378	0.00642
Sm^{3+}	4.8	27568	26230	$^4H_{5/2} \rightarrow {}^4F_{9/2}$	0.01291	0.98709	0.11362	1.30788	0.00644
		26702	25843	$^4H_{5/2} \rightarrow {}^6P_{5/2}$	0.01622	0.96783	0.12736	1.67591	0.01596
		24876	24483	$^4H_{5/2} \rightarrow {}^4I_{3/2}$	0.01580	0.98420	0.12570	1.60536	0.00787

*Hypersensitive bands

50.89, 53.99, 55.03, 55.49, 57.63, 59.17 and 59.48 ppm for piperazine ring. The methoxy carbon of *o*-vanillin exists at 54.16 ppm in the spectra of Schiff base and its Ln(III) complexes.

Thermal analysis: The TG-DTA measurements of Ln(III) complexes were carried out in the air and thermal data are given in Table-4. The synthesized Ln(III) complexes containing piperazine based Schiff base (L_2) show the thermal decomposition in three steps. The first step shows an endothermic peak in the order of 140-180 ºC due to the dehydration of two coordinated water molecules.

The formation of Ln(III) nitrates shows the second step in TG-DTA measurements was the decomposition of the ligand from Ln(III) complexes in the range of temperature at 180-350 ºC. In the end, the most stable corresponding lanthanum oxides were formed [16]. The phases involved in the thermal decomposition of Ln(III) complexes are specified as follows:

$$[Ln(L_2)(H_2O)_2(NO_3)]NO_3 \xrightarrow[140\text{-}180\ ^\circ C]{-2H_2O} [Ln(L_2)(NO_3)_2]$$

$$\xrightarrow[180\text{-}350\ ^\circ C]{-L_2} Ln(NO_3)_2 \xrightarrow[350\text{-}750\ ^\circ C]{} Ln_2O_3$$

Powder X-ray diffraction studies: The X-ray powder diffraction patterns for complexes are illustrated in Fig. 2a-f. Based on the spectra, it is evident that all the synthesized six Ln(III) complexes exhibit isomorphous structural units.

Photoluminescence spectra: The photoluminescence was recorded for free ligand (L_2) and its Pr(III), Nd(III) and Sm(III) complexes. Among these Sm(III) complexes only show radi-ation in the range 560 nm and 590 nm. The peak at 560 nm is green radiation due to the transition $^4G_{5/2} \rightarrow {}^6H_{3/2}$ of Sm^{3+} ions [18]. A yellow emission peak at 590 nm is due to the transition $^4G_{5/2} \rightarrow {}^6H_{5/2}$ of Sm^{3+} ions. The green radiations are a hypersensitive band which has a higher electric dipole character while the yellow radiation has a higher magnetic dipole character. The results also showed that the free ligand (L_2), Pr(III) and Nd(III) compounds did not show luminescence property whereas SmL_2 complexes exhibit luminescence due to the transition of Sm^{3+} ion (Fig. 3).

Antimicrobial activity: Uncoordinated Schiff base shows the zone of inhibition of 13-17 mm against four species. The standard drug clotrimazole exhibit zone of inhibition values in the range of 22-34 mm. Ln(III) complexes exhibits zone of

TABLE-4
THERMAL DATA OF Ln(III) NITRATE COMPLEXES CONTAINING SCHIFF BASE LIGAND (L_2)

Complexes	DTA temperature (°C)	Thermogravimetry temperature range (°C)	Weight loss (%)		Nature of the reaction
			Observed	Calculated	
La^{3+}	(+)172.73	150-180	6.42	6.5	Dehydration
	(+)277.92	180-340	46.4	46.5	Loss of ligand
	(–)496.58	340-750	69.3	69.3	Decomposed to metal oxide
Ce^{3+}	(+)153.31	140-180	6.4	6.5	Dehydration
	(+)268.75	180-350	46.4	46.7	Loss of ligand
	(–)522.11	350-750	69.3	69.3	Decomposed to metal oxide
Pr^{3+}	(+)147.11	140-160	6.4	6.5	Dehydration
	(+)276.55	160-340	46.4	46.8	Loss of ligand
	(–)502.44	340-750	69.9	69.6	Decomposed to metal oxide
Nd^{3+}	(+)148.37	140-170	6.4	6.2	Dehydration
	(+)267.07	170-340	46.1	46.4	Loss of ligand
	(–)536.87	340-750	70.2	70.2	Decomposed to metal oxide
Sm^{3+}	(+)173.08	150-180	6.4	6.1	Dehydration
	(+)274.94	180-350	45.9	46.0	Loss of ligand
	(–)498.64	350-750	69.2	69.4	Decomposed to metal oxide
Gd^{3+}	(+)166.42	150-170	6.2	6.5	Dehydration
	(+)272.21	170-340	45.1	45.4	Loss of ligand
	(–)487.24	340-750	68.5	68.0	Decomposed to metal oxide

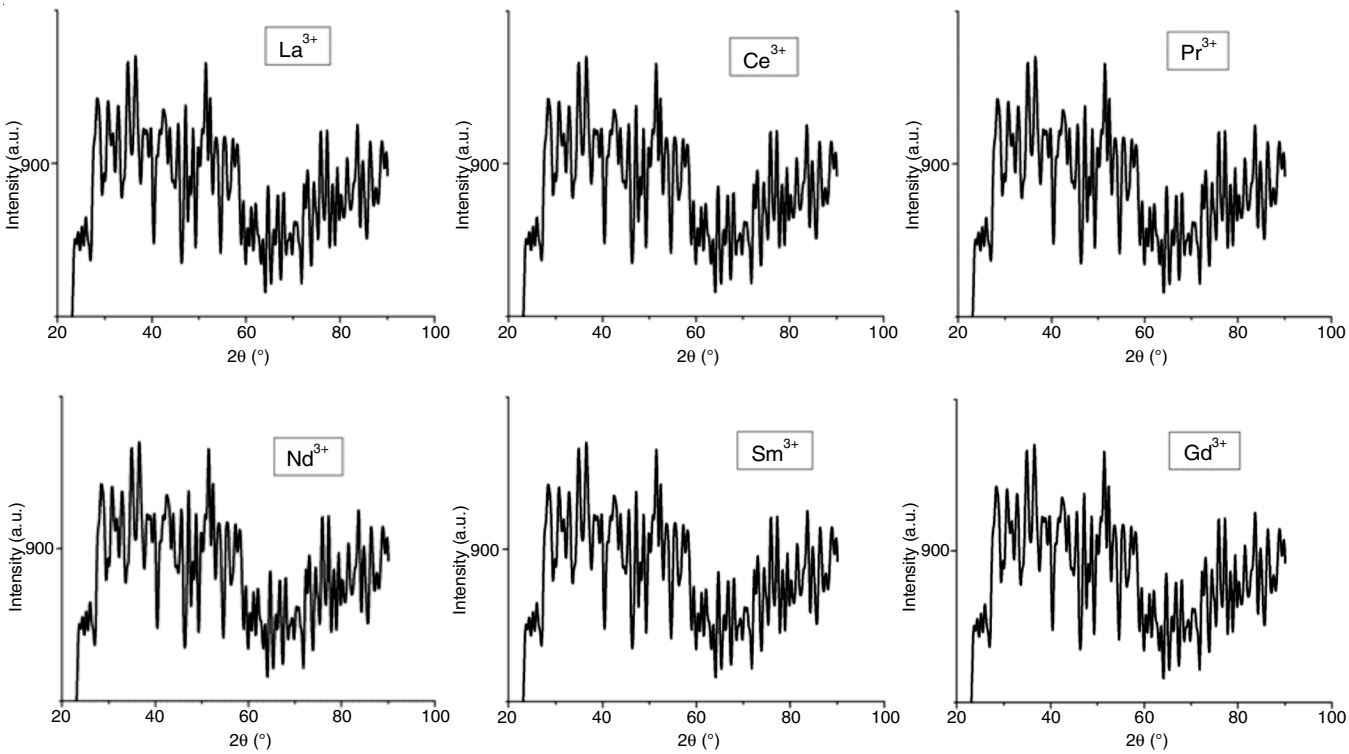

Fig. 2. XRD diffraction pattern of (a) lanthanum(III) complex; (b) cerium(III) complex; (c) praseodymium(III) complex; (d) neodymium(III) complex; (e) samarium(III) complex; (f) gadolinium(III) complex

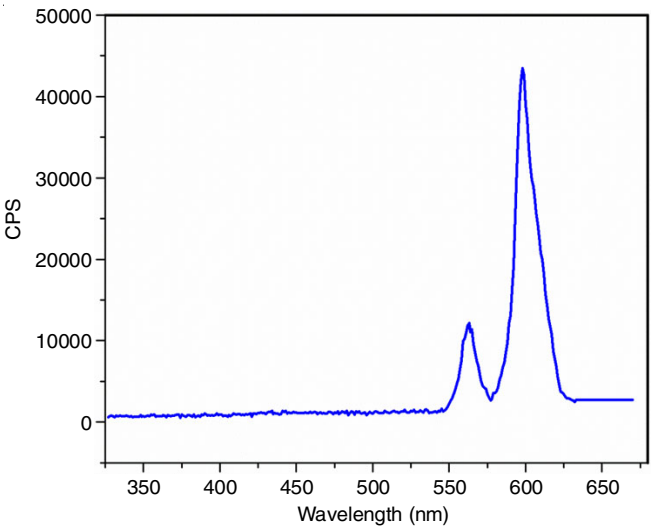

Fig. 3. Photoluminescence spectrum of samarium(III) complex (SmL_2)

inhibition values around 12-22 mm (Table-5). The results exposed that the complexes show the greater activity than the free ligand and lesser activity than the standard drugs.

The antifungal activity of the free ligand (L_2) and its Ln(III) complexes were evaluated and the results are represented in Table-6. The free ligand (L_2) shows the zone of inhibition in the range 10 and 12 mm against *C. albicans* and *A. niger*. The Ln(III) complexes show 9-13 mm against *C. albicans* and 15-17 mm against *A. niger*. The standard drug clotrimazole shows 10 and 24 mm against *C. albicans* and *A. niger*. The results indicated that the complexes show slightly higher activity than the free ligand and lesser activity than standard drugs.

Anticancer activity of piperazine Schiff base (L2) and its Ln(III) complexes: The results of anticancer activity of Schiff base ligand (L_2) and its Ln(III) complexes are shown in Table-7. The free Schiff base ligand (L_2) shows cytotoxicity from 25 to 100 µM. At 6.25 and 12.5 µM, the ligand did not exhibit a cytotoxic effect whereas the percentage of cell growth was above 80% (Fig. 4). At 50 µM cytotoxicity of the free ligand, the percentage of cell growth was 73%. At 100 µM, the free ligand displays cytotoxicity than other concentrations cell viability around 50%. The cytotoxicity of the complexes started from 50 µM, the cell viability around 61-68%. All Ln(III) complexes exhibit better cytotoxicity at 100 µM, cell viability

TABLE-5
ANTIBACTERIAL ACTIVITY DATA OF PIPERAZINE SCHIFF BASE LIGAND (L_2) AND ITS Ln(III) NITRATE COMPLEXES

Organisms	Standard ciprofloxacin (10 µg/disc)	Zone of inhibition (mm); Sample-I (100 µg/disc)						
		L_2	La^{3+}	Ce^{3+}	Pr^{3+}	Nd^{3+}	Sm^{3+}	Gd^{3+}
Staphylococcus aureus	30	13	20	17	15	16	20	19
Bacillus subtilis	26	17	18	19	19	18	21	18
Escherichia coli	25	14	17	17	17	16	23	20
Pseudomonas aeruginosa	28	13	18	17	16	17	20	17

TABLE-6
ANTIFUNGAL ACTIVITY OF PIPERAZINE SCHIFF BASE LIGAND (L_2) AND ITS Ln(III) COMPLEXES

Organisms	Standard clotrimazole 10 µg/disc	Zone of inhibition (mm); Sample-I (100 µg/disc)						
		L_2	LaL_2	CeL_2	PrL_2	NdL_2	SmL_2	GdL_2
C. albicans	10	10	9	9	12	13	9	9
A. niger	24	12	17	17	15	17	17	17

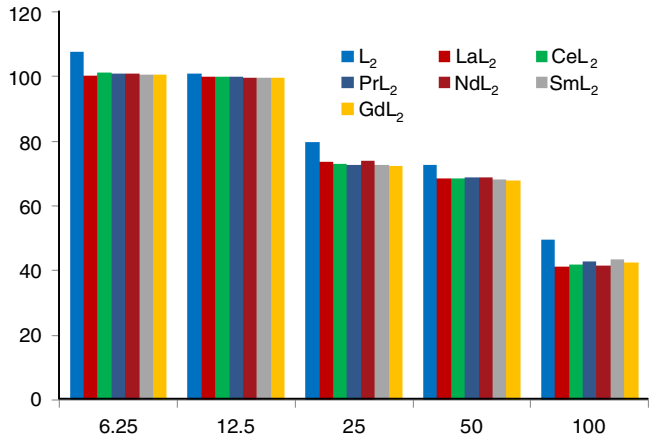

Fig. 4. Effect of concentration of anticancer activity of piperazine Schiff base ligand (L_2) and its Ln(III) complexes on the percentage of cell viability against MCF-7 cell lines

around 41-43%. The results showed that the free ligand (L_2) and its Ln(III) complexes exhibit cytotoxicity at 100 µM. The Ln(III) complexes exhibit slightly greater cytotoxicity than the free ligand (Fig. 5).

Conclusion

This study showed the successful synthesis of Schiff base and its La(III), Ce(III), Pr(III), Nd(III), Sm(III) and Gd(III) complexes, which were characterized using IR, UV, NMR, TG-DTA, X-ray diffraction and photoluminence studies. All the complexes were 1:1 electrolytes. Among the two nitrate ions, one of them coordinated to the Ln^{3+} ions in bidentate manner and another appeared as ionic nitrate. Two water molecules coordinated with Ln^{3+} ions (Fig. 6). All the complexes containing one Schiff base ligand (L_2) which is coordinated through phenolic oxygen, imine nitrogen and two piperazine ring nitrogen, indicate that the ligand act as tetradentate and also complexes are isostructural. Finally, the coordination number of Ln(III) complexes is nine. The results also indicate that the biological activity increases on complexation. Lanthanide(III) complexes of Schiff base show greater inhibitory action towards the human breast cancer cell line (MCF-7).

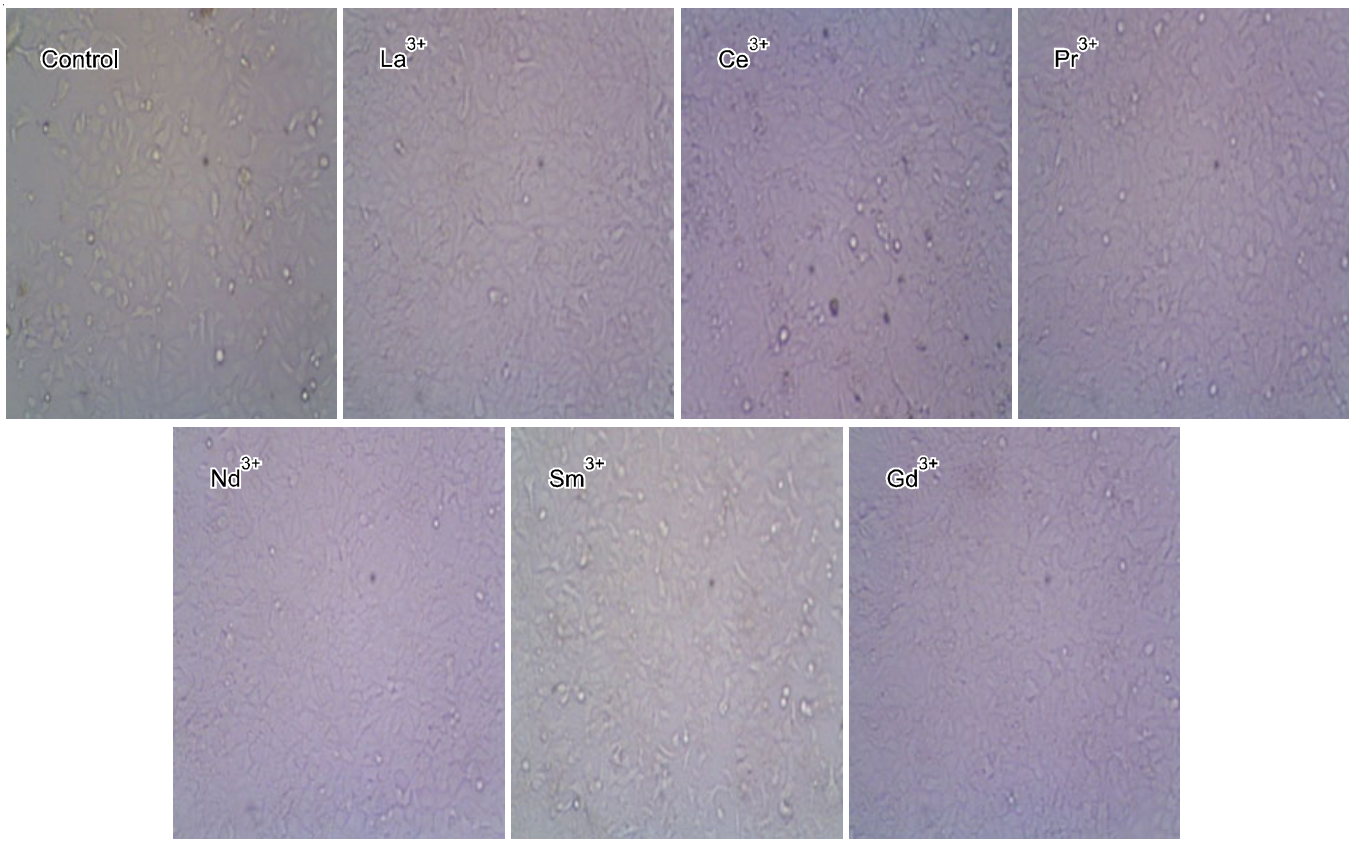

Fig. 5. Cells treated with Ln(III) complexes (100 µM) containing piperazine Schiff base ligand (L_2) exhibit characteristic morphological changes of apoptosis. Control or treated MCF-7 cells were incubated in culture dishes. After 48 h treatment the dishes were observed under phase contrast and morphology was photographed

TABLE-6
ANTIFUNGAL ACTIVITY DATA OF PIPERAZINE SCHIFF BASE LIGAND (L_2) AND ITS Ln(III) COMPLEXES

Organisms	Standard clotrimazole (10 µg/disc)	Zone of inhibition (mm); Sample-I (100 µg/disc)						
		L_2	La^{3+}	Ce^{3+}	Pr^{3+}	Nd^{3+}	Sm^{3+}	Gd^{3+}
Candida albicans	10	10	9	9	12	13	9	9
Aspergillus niger	24	12	17	17	15	17	17	17

TABLE-7
ANTICANCER ACTIVITY DATA OF PIPERAZINE SCHIFF BASE (L_2) AND ITS Ln(III) COMPLEXES

Concentration (µM)	Cell growth (%)						
	L_2	La^{3+}	Ce^{3+}	Pr^{3+}	Nd^{3+}	Sm^{3+}	Gd^{3+}
6.25	107.6523	100.0923	100.9906	100.7279	100.6865	100.5276	100.6267
12.5	100.7686	99.82676	99.72671	99.86721	99.68612	99.56786	99.52326
25	79.5276	73.62571	72.86617	72.56671	73.86517	72.52761	72.43321
50	72.72414	68.52762	68.63271	68.72612	68.86612	67.99723	67.73221
100	49.72676	41.12231	41.97671	42.98627	41.56767	43.56761	42.52312

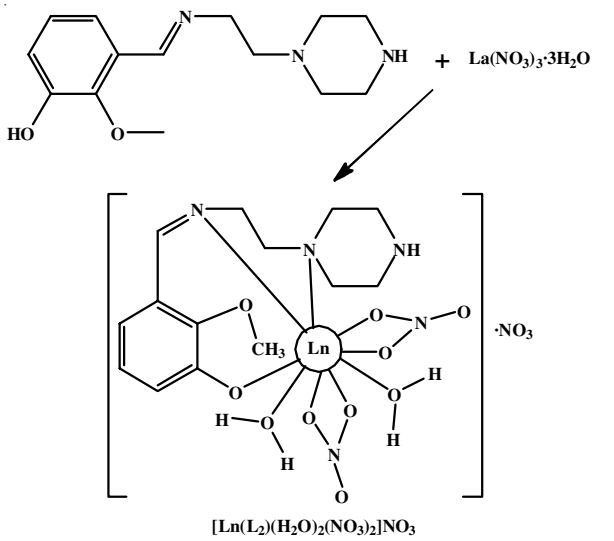

Fig. 6. General structures of Ln(III) complexes where Ln = La, Ce, Pr, Nd, Sm and Gd

CONFLICT OF INTEREST

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

REFERENCES

1. A. Catalano, M.S. Sinicropi, D. Iacopetta, J. Ceramella, A. Mariconda, C. Rosano, E. Scali, C. Saturnino and P. Longo, *Appl. Sci.*, **11**, 6027 (2021); https://doi.org/10.3390/app11136027
2. L.-E. Niu, Y. Yang, X.-H. Qi and X. Liang, *Synth. React. Inorg. Metal-Org. Nano-Metal Chem.*, **39**, 1 (2009); https://doi.org/10.1080/15533170802665419
3. Y.S. Song, B. Yan and L.H. Weng, *Polyhedron*, **26**, 4591 (2007); https://doi.org/10.1016/j.poly.2007.06.018
4. M.C. Suen, T.C. Keng and J.C. Wang, *Polyhedron*, **21**, 2705 (2002); https://doi.org/10.1016/S0277-5387(02)01284-6
5. S.V. Ganesan and S. Natarajan, *Inorg. Chem.*, **43**, 198 (2004); https://doi.org/10.1021/ic034836p
6. H. Xu, Y. Song, L. Mi, H. Hou, M. Tang, Y. Sang, Y. Fan and Y. Pan, *Dalton Trans.*, **6**, 838 (2006); https://doi.org/10.1039/B508177G
7. X.-J. Zhao, M. Du, Y. Wang and X.-H. Bu, *J. Mol. Struct.*, **692**, 155 (2004); https://doi.org/10.1016/j.molstruc.2004.01.025
8. S.A. Khan, S.A. Bhat, S.A.A. Nami, A. Kareem and N. Nishat, *Comptes Rendus Chim.*, **21**, 872 (2018); https://doi.org/10.1016/j.crci.2018.07.003
9. M. Leopoldo, E. Lacivita, N.A. Colabufo, M. Contino, F. Berardi and R. Perrone, *J. Med. Chem.*, **48**, 7919 (2005); https://doi.org/10.1021/jm050729o
10. D. Askin, K.K. Eng, K. Rossen, R.M. Purick, K.M. Wells, R.P. Volante and P.J. Reider, *Tetrahedron Lett.*, **35**, 673 (1994); https://doi.org/10.1016/S0040-4039(00)75787-X
11. J. Su, H. Tang, B.A. McKittrick, D.A. Burnett, H. Zhang, A. Smith-Torhan, A. Fawzi and J. Lachowicz, *Bioorg. Med. Chem. Lett.*, **16**, 4548 (2006); https://doi.org/10.1016/j.bmcl.2006.06.034
12. W.J. Geary, *Coord. Chem. Rev.*, **7**, 81 (1971); https://doi.org/10.1016/S0010-8545(00)80009-0
13. A.K. Rathi, R. Syed, H.-S. Shin and R.V. Patel, *Expert Opin. Ther. Pat.*, **26**, 777 (2016); https://doi.org/10.1080/13543776.2016.1189902
14. Z. Chen, Y. Wu, D. Gu and F. Gan, *Dyes Pigments*, **76**, 624 (2008); https://doi.org/10.1016/j.dyepig.2006.11.009
15. A. Kilic, I. Tegin, E. Tas and R. Ziyadanogullan, *J. Iran. Chem. Soc.*, **8**, 68 (2011); https://doi.org/10.1007/BF03246203
16. H. Icbudak, V.T. Yilmaz and H. Ölmez, *J. Therm. Anal. Calorim.*, **53**, 843 (1998); https://doi.org/10.1023/A:1010190701136
17. A. Altomare, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, R. Rizzi and P.-E. Werner, *J. Appl. Cryst.*, **33**, 1180 (2000); https://doi.org/10.1107/S0021889800006427
18. T. Yu, K. Zhang, Y. Zhao, C. Yang, H. Zhang, D. Fan and W. Dong, *Inorg. Chem. Commun.*, **10**, 401 (2007); https://doi.org/10.1016/j.inoche.2006.12.010
19. P.K. Sharma, *Asian J. Pharm. Clin. Res.*, **10**, 47 (2017); https://doi.org/10.22159/ajpcr.2017.v10i2.15673
20. S. Bhati, V. Kumar, S. Singh and J. Singh, *J. Mol. Struct.*, **1191**, 197 (2019); https://doi.org/10.1016/j.molstruc.2019.04.106
21. B. Kapoor, A. Nabi, R. Gupta and M. Gupta, *Asian J. Pharm. Clin. Res.*, **10**, 7 (2017); https://doi.org/10.22159/ajpcr.2017.v10s4.21329
22. A. Rawat, A. Kaur and H. Kaur, *Asian J. Chem.*, **29**, 2084 (2017); https://doi.org/10.14233/ajchem.2017.20832
23. W.W. Slater and I.E. Thow, Aqueous Solution of Salts of 1,4-*bis*(2-Hydroxypropyl)-2-methyl piperazine and Epoxy Ester-Maleic Anhydride Adducts, US Patent, US 3397159 (1968).
24. M. AI-Ghorbani, *J. Chem. Pharm. Res.*, **5**, 281 (2015).
25. O.A. Phillips, E.E. Udo and S.M. Samuel, *J. Med. Chem.*, **43**, 1095 (2008); https://doi.org/10.1016/j.ejmech.2007.07.006