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Synthesis, characterisation and antimicrobial studies on thorium(IV) and cerium((IV) complexes of vanillin schiff bases of diamines

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ABSTRACT

A new Series of rare earth metal complexes of Th(IV) and Ce(IV) with schiff bases formed from Vanillin and diamines such as ethylene diamine(en), diethylene triamine(dien), triethylene tetramine(trien) (the Schiff bases viz vanen, vandien and vantrien respectively) have been synthesized and characterized by elemental and thermal analysis, UV-Vis, IR,EPR Spectral studies and magnetic susceptibility studies. In order to evaluate the effect of Th(IV) and Ce(IV) Schiff base complexes they have been screened for antibacterial, antifungal and anticancer activities which show promising activity towards some of the tested microorganisms and colon cancer cells

Keywords: Thorium(IV) and cerium((IV) vanillin schiff base complexes - antibacterial, Antifungal and anticancer studies.

1. INTRODUCTION

Schiff bases are a versatile class of ligands which are extensively studied in recent years. Metal complexes of Schiff bases exhibit a broad range of biological activities which includes antifungal, antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral and antipyretic. They also find applications in agriculture and industrial fields [1-5]. Aromatic schiff bases and their metal complexes catalyse reactions such as oxygenation [6,7], hydrolysis [8], electro-reduction [9] and decomposition. The coordination behavior of Schiff base ligand with rare earth metals such as Lanthanides and actinides have attracted a great deal of interest because of applications in medical diagnosis and material science. In medicine, lanthanide complexes are exploited as constrast agents [10-12] for magnetic resonance imaging(MRI) and are gaining significance in other diagnostic procedures [13] and are used as radiotherapeutic drugs [14]. The present study describes the synthesis, spectroscopic characterization and antibacterial, antifungal and anticancer activities of Ce(IV) and Th(IV) schiff base complexes.

2. EXPERIMENTAL

2.1. Chemicals and reagents

All Chemicals used were of analytical grade and used without purification. All reagents were purchased from merck. The Thorium nitrate, ceric ammonium nitrate and vanillin used were of AR grade while ethylene diamine, diethylenetriamine and triethylene tetramine are pure grade chemicals from Merck.

2.2. Method

Schiff base complexes were prepared by adding 1mmol of ethylene diamine/diethylene triamine/triethylene tetramine in 10ml of ethanol, to 2mmol of Vanillin in the presence of aqueous solution of Ceric ammonium nitrate / Throium nitrate(1mmol) with continuous stirring for 10 minutes. The formed yellow precipitate was filtered off ,washed with water and alcohol several times and dried in vaccum. The metal content in the complexes was determined by optical emission spectroscopy using ICP-OES Perkin Elmer optima 5300 DV Spectrometer and Nitrogen was estimated by Kjelhdhal's method. TGA were recorded in nitrogen atmosphere using NETZSCH STA 409 C/CD thermal analyzer with a heating rate of 10°C/min. Magnetic susceptibility studies were carried out using Vibrating magnetometer EG and GPARC model 155. UV – Visible absorption spectra were done using Varian Cary Spectrophotometer 5E – UV-Vis-NIR. The IR spectra were recorded in KBr using Schimadzu IR spectrometer. Antibacterial and antifungal activities of Vanillin-en/dien/trien Schiff base complexes of Th(IV) andCe(IV) were studied using a minimum modification of the disc diffusion method originally described by Bauer [15]. The

invitro cytotoxicity of the prepared complexes was determined by MTT-based assay with colon cancer cell line (HT 29). In parallel the activity was tested on monkey kidney cells (normal cell line VERO [16].

3. RESULTS AND DISCUSSION

The elemental analysis data furnished in table 1, confirms the proposed structure. The IR spectral data (Table 2) shows a peak around 1590 cm-1 confirming the presence of –C=N- bond and the formation of Schiff base. A band around 3400 cm-1 indicates the –O-H. The bands around 3069 cm-1 and 2945 cm-1 are assigned to the stretching of aromatic –C-H of the vanillin ring and aliphatic C-H stretching of the amine. The electronic spectral data on the complexes (Table –I) show two bands in the region 375-420 nm for Ce(IV)] and 280-316 nm for Th(IV) complexes which may be assigned to ligand to metal charge transfer(CT) transitions often encountered in these type of complexes. The NMR spectral data of the complexes is furnished in table 3. The signal in the region around 3.7 in the vanen Schiff base complex is assigned to the Methylenic protons while they appear in the region 1.2-1.4 ppm in vandien and vantrien complexes as a triplet.The aromatic protons of vanillin appear between 6.7-7.5 ppm . The –CH=N proton appears as a quartet around 4.3 ppm. The methoxy group protons present in vanillin appear in the region 3.8-4.3 ppm as a doublet.This may be interpreted as arising due to coupling between imine and methoxy protons. The secondary amino group NH protons present in the diamine moiety of dien and trien appearsround a 7.8 ppm. Protons corresponding to coordinated –OH appear around 10 ppm.

3.1. Antimicrobial activity

The details of bactericidal and fungicidal activity of the complexes are furnished in table 4 and table 5 respectively. All the complexes are found to show moderate activity against the following bacteriae viz: *E.coli, Pseudomonas aeroginosa, Staphylococcus aureus, Bacillus spp and Vibrio parahaemolytics /salmonella spp* and following fungi viz: *Candida albicans, Aspergillus flavors, Pencillium spp., Aspergillus niger* and *Trichophyton*. Among the six complexes, Th(IV) complexes were found to be least active against the *E.Coli* and *Vibrio parahaemolytics* The Ce(IV) complexes of en and dien show better activity towards *Staphylococcus aureus* than trien analogue. The trend is found to be reversed in the Th(IV) complexes. The Th (en) complexes show better activity against *Staphylococcus aureus* whereas the dien and trien complexes show lower activity. In the case of fungicidal activity, the Th complexes in general show superior activity than the Ce complexes. All the Ce complexes show moderate activity only at high concentrations .In general the complexes are highly active against Candida albicans.

3.2. Anticancer activity

The anticancer behavior of the complexes is presented in figures 1 – 6. All the complexes show a decent activity against the HT-29 cell line and the activity was compared against the VERO (normal) cell line which indicated the complexes considerably destroy normal cells too.

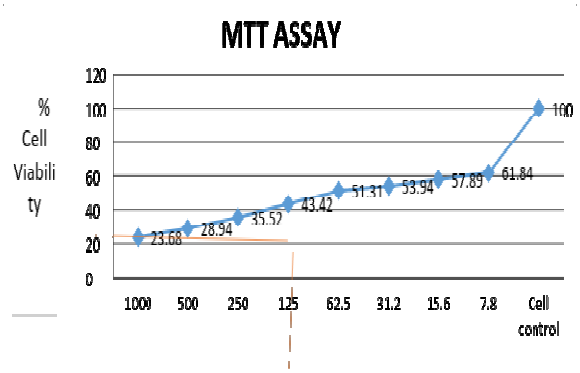

Figure - 1: Anticancer effect of [Th(vanen-2H) $_2$(OH) $_2$] onHT-29 Cell line.

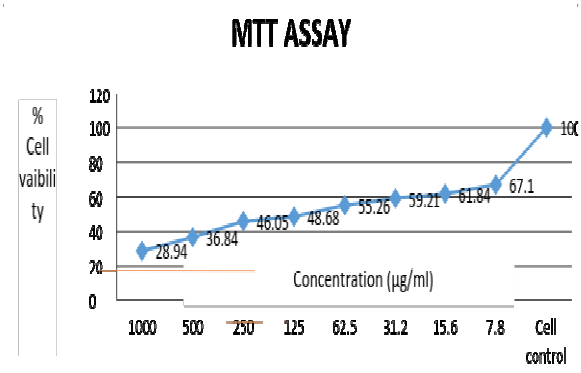

Figure – 2: Anticancer effect of [Th(vandien-2H) $_2$(OH) $_2$] onHT-29 Cell line.

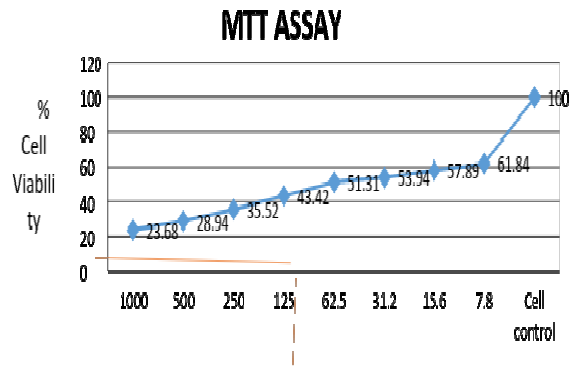

Figure - 3: Anticancer effect of [Th(vantrien-2H) (OH) $_2$] onHT-29 Cell line.

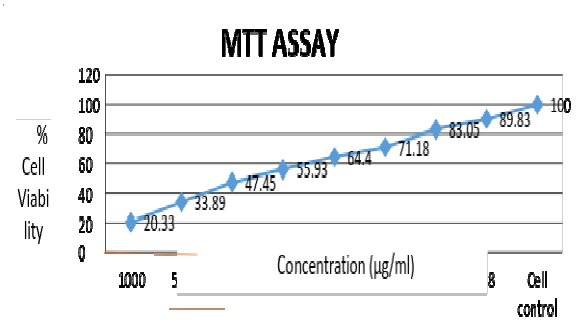

Figure - 4: Anticancer effect of [Ce (vanen-2H) (OH) $_2$] onHT-29 Cellline.

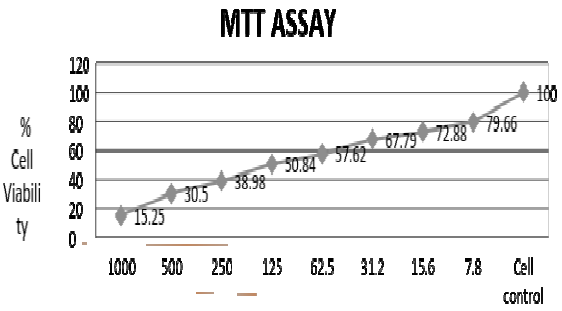

Figure - 5: Anticancer effect of [Ce(vandien-2H) (OH) $_2$] onHT-29 Cell line.

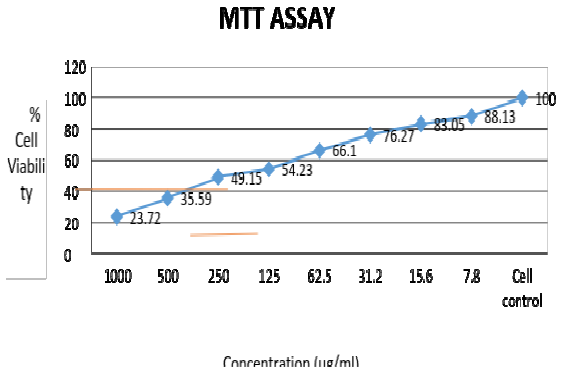

Figure – 6: Anticancer effect of [Ce(vantrien-2H) (OH) $_2$] onHT-29 Cell line.

Table - 1: Elemental analysis data and uv-visible absorption spectra of the complexes

Compelexes	% metal		% metal oxide		% nitrogen		uv-vis λmax (nm)
	Exp	Theo	Exp	Theo	Exp	Theo	
[Th (vanen-2H) $(OH)_2$]	40.42	39.17	43.86	44.57	4.56	4.73	359, 310, 280
[Th(vandien-2H) $(OH)_2$]	36.90	36.52	42.30	41.56	7.19	6.61	310, 280
[Th(vantrien-2H)$(OH)_2$]	33.43	34.20	40.39	38.92	9.01	8.26	316, 281
[Ce (vanen-2H) $(OH)_2$]	28.58	27.99	35.01	34.39	4.85	5.60	379, 400
[Ce (vandien-2H) $(OH)_2$]	26.32	25.78	32.23	31.67	7.76	7.73	375, 400
[Ce(vantrien-2H) $(OH)_2$]	24.40	23.89	30.42	29.35	10.02	9.53	385, 420

TABLE - 2: IR spectral data of the complexes(cm^{-1})

Complexes	υ_{OH}	υ_{CH} (aro)	υ_{CH} (ali)	δ M-OH	$\upsilon_{C=N}$
[Th (vanen-2H) $(OH)_2$]	3428	3069	2986, 2949	1665	1587
[Th (vandien-2H) $(OH)_2$]	3437	3065	2943, 2832	1665	1587
[Th (vantrien-2H) $(OH)_2$]	3439	3065	2988, 2953	1665	1587
[Ce (vanen-2H) $(OH)_2$]	3408, 3397	3067	2988, 2947	1658	1589
[Ce (vandien-2H) $(OH)_2$]	3426, 3412	3067	2986, 2955	1660	1587
[Ce (vantrien-2H) $(OH)_2$]	3395	3005	2940	1664	1589

Table - 3: ^{1}HNMR spectral data on the complexes-Chemical shift in ppm

Complexes	CH_2 - Amine	OCH_3 Vanillin	Imine proton	Aromatic protons	N-H	OH-
[Th(vanen-2H)$(OH)_2$]	3.77t	3.85d	4.35q	6.8, 7.2, 7.3, 7.4.	-	9.61, 9.8
[Th(vandien-2H)$(OH)_2$]	1.28t	3.7d	4.35q	6.75, 7.2, 7.3, 7.4.	7.75	9.67, 9.62
[Th(vantrien-2H)$(OH)_2$]	1.283(t)	3.85d	4.35q	7.00,7.25, 7.35,7.5	7.9	9.65,9.85
[Ce (vanen-2H) $(OH)_2$]	3.6t	3.75d	4.3q	6.8,7.2,7.4	-	10.1,10.8
[Ce (vandien-2H)$(OH)_2$]	1.28t	3.9 d	4.35q	6.8,7.0,7.6	7.75	9.8
[Ce(vantrien-2H) $(OH)_2$]	1.05t(4H) 1.35t(8H)	3.76d	4.3q	6.7,7.1,7.3	7.75	9.8, 10.6

Table - 4: Antibacterial studies

Complexes	Organisms	Zone of Inhibition (mm)			Antibiotic (1mg/mL)	DMSO (20µl)
	Concentration(µg/mL)	1000	750	500		
[Th (vanen-2H) $(OH)_2$]	*E.coli*	8 mm	6 mm	4 mm	15 mm	-
	Pseudomonas aeroginosa	10 mm	7 mm	4 mm	14 mm	-
	Staphylococcus aureus	12 mm	10 mm	8 mm	16 mm	-
	Bacillus spp.	12 mm	10 mm	7 mm	15 mm	-
	Vibrio parahaemolytics	8 mm	6 mm	5 mm	13 mm	-
[Th (vandien-2H) $(OH)_2$]	*E.coli*	7 mm	6 mm	3 mm	12mm	-
	Pseudomonas aeroginosa	6 mm	5 mm	3 mm	11 mm	-
	Staphylococcus aureus	7 mm	5 mm	3 mm	13 mm	-
	Bacillus spp.	9 mm	6 mm	4 mm	14 mm	-
	Vibrio parahaemolytics	6 mm	5 mm	4 mm	10 mm	-
[Th (vantrien-2H) $(OH)_2$]	*E.coli*	8 mm	6 mm	4 mm	12 mm	-
	Pseudomonas aeroginosa	9 mm	6 mm	4 mm	13 mm	-
	Staphylococcus aureus	9 mm	7 mm	5 mm	12 mm	-
	Bacillus spp.	13 mm	10 mm	8 mm	17 mm	-
	Vibrio parahaemolytics	6 mm	5 mm	4 mm	10 mm	-
[Ce (vanen-2H) (OH)2]	*E.coli*	15 mm	10 mm	6 mm	25 mm	-
	Pseudomonas aeroginosa	10 mm	8 mm	4 mm	28mm	-
	Staphylococcus aureus	8 mm	6 mm	3 mm	25 mm	-
	Bacillus spp.	16 mm	13 mm	9 mm	30 mm	-
	Salmonella spp.	20 mm	15 mm	6 mm	26 mm	-
[Ce (vandien-2H) (OH)2]	*E.coli*	13 mm	8 mm	4 mm	24 mm	-
	Pseudomonas aeroginosa	10 mm	6 mm	5 mm	27 mm	-
	Staphylococcus aureus	9 mm	7 mm	5 mm	20 mm	-
	Bacillus spp.	13 mm	11 mm	8 mm	30 mm	-
	Salmonella spp.	11 mm	9 mm	8 mm	25 mm	-
[Ce (vantrien-2H) (OH)2]	*E.coli*	9 mm	7 mm	5 mm	18 mm	-
	Pseudomonas aeroginosa	14 mm	12 mm	6 mm	20 mm	-
	Staphylococcus aureus	17 mm	11 mm	9 mm	19 mm	-
	Bacillus spp.	16 mm	11 mm	8 mm	25 mm	-
	Salmonella spp.	17 mm	12 mm	9 mm	26 mm	-

Table - 5: Antifungal studies

Complexes	Organisms	Zone of Inhibition (mm)			Antibiotic (1mg/mL)	DMSO (20µL)
	Concentration(µg/mL)	1000	750	500		
[Th (vanen-2H) $(OH)_2$]	*Candida albicans*	7 mm	6 mm	5 mm	8 mm	-
	Aspergillus flavors	7 mm	7mm	6mm	10mm	-
	Pencillium spp.	10 mm	7 mm	6 mm	10 mm	-
	Aspergillus niger	5 mm	4 mm	4mm	5mm	-
	Trichophyton	6 mm	4 mm	4 mm	7 mm	-
[Th (vandien-2H) $(OH)_2$]	*Candida albicans*	6 mm	5 mm	4 mm	7 mm	-
	Aspergillus flavors	6 mm	5 mm	5 mm	8 mm	-
	Pencillium spp.	6 mm	6 mm	5 mm	10 mm	-
	Aspergillus niger	3mm	2 mm	1 mm	5 mm	-
	Trichophyton	6 mm	5 mm	5 mm	6 mm	-
[Th (vantrien-2H) $(OH)_2$]	*Candida albicans*	6mm	5mm	4mm	7mm	-
	Aspergillus flavors	9 mm	7 mm	6 mm	10mm	-
	Pencillium spp.	7 mm	7 mm	6 mm	10 mm	-
	Aspergillus niger	7 mm	5 mm	4 mm	5 mm	-
	Trichophyton	6 mm	6 mm	5 mm	7 mm	-
[Ce (vanen-2H) $(OH)_2$]	*Candida albicans*	6 mm	5 mm	3 mm	9 mm	-
	Aspergillus flavors	5 mm	3 mm	1 mm	8 mm	-
	Pencillium spp.	3 mm	2 mm	1 mm	5 mm	-
	Aspergillus niger	4 mm	2 mm	1 mm	6 mm	-
	Trichophyton	5 mm	3 mm	2 mm	6 mm	-
[Ce (vandien-2H) $(OH)_2$]	*Candida albicans*	5 mm	2 mm	1 mm	6 mm	-
	Aspergillus flavors	3 mm	1 mm	1 mm	5 mm	-
	Pencillium spp.	4 mm	2 mm	1 mm	4 mm	-
	Aspergillus niger	3 mm	1 mm	1 mm	5 mm	-
	Trichophyton	6 mm	4 mm	1 mm	9 mm	-
[Ce (vantrien-2H) $(OH)_2$]	*Candida albicans*	7 mm	4 mm	2 mm	9 mm	-
	Aspergillus flavors	5 mm	2 mm	1 mm	6 mm	-
	Pencillium spp.	6 mm	3 mm	2 mm	5 mm	-
	Aspergillus niger	4 mm	1 mm	1 mm	5 mm	-
	Trichophyton	4 mm	3 mm	1 mm	5 mm	-

4. CONCLUSION

The complexes, from the above elemental and spectral analysis,are proposed to have a distorted octahedral geometry with a tetradentate deprotanated Schiff base ligand coordinating through the imine N atoms and O^- of vanillin residue. Two OH^- ions satisfy two more coordination sites.. The antimicrobial studies and the anticancer studies show promising applications in the field of medicines but damage to normal cells should be checked with systematic variations of ligands and metal ion.

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