

Coordination Studies and Biological Screening of Cerium(III) Complexes Derived from an Azomethine Schiff Base and Amino Acids

Uttam N. Dhaigude¹, Nikita U. Dhaigude¹, Kirti J. Mhatre², Ganesh A. Thakur³

¹Department of Chemistry, Mahatma Phule Arts, Science and Commerce College, Panvel, Maharashtra, India.

²Department of Biotechnology, Mahatma Phule Arts, Science and Commerce College, Panvel, Maharashtra, India.

³Principal and Research Guide, Mahatma Phule Arts, Science and Commerce College, Panvel, Maharashtra, India.

Abstract: Three new mixed ligand cerium (III) complexes with Schiff base (DBAP) derived from 2-aminophenol and 4-dimethylaminobenzaldehyde as a primary ligand and L-valine, L-isoleucine, L-phenylalanine, as secondary ligands have been synthesized. All synthesized cerium complexes were characterized by using different tools like elemental analysis, magnetic susceptibility study, conductivity measurements, infrared and electronic spectroscopic methods. The infrared spectroscopic study showed that bidentate Schiff base and amino acid ligands coordinated to Cerium metal ion through oxygen and nitrogen atoms respectively. The metal-ligand interaction was studied by electronic spectral technique. Magnetic susceptibility measurements revealed paramagnetic nature of synthesized complexes. The antibacterial activity of Schiff base ligand and complexes were studied by agar cup method against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, and *Shigella sonnei* bacteria. It was found that synthesized cerium metal complexes showed remarkable antibacterial activity as compared to cerium salt and free ligands.

Keywords: Mixed ligand complex, 2-aminophenol, amino acids, 4-dimethylamino benzaldehyde, Antibacterial activity

I. INTRODUCTION

The Schiff bases are imine or azomethine compounds formed by the condensation of active carbonyl compounds with primary amines. The Schiff bases plays vital roles in medicinal inorganic chemistry due to their excellent biological applications such as antimicrobial, anticancer, antiviral and antioxidant properties [1, 2]. Numerous studies have shown that mixed ligand transition metal complexes derived from Schiff bases possess notable antifungal and antibacterial effects [3,4]. The biological and catalytic activities, including antioxidant and antimicrobial effects, of lanthanide complexes derived from the salicylaldehyde-2-picolinoylhydrazone Schiff base ligand have been studied [5]. The inner transition metal complexes with Schiff base possesses good cytotoxic, antifungal, and antibacterial activities [6-8]. The synthesis and characterization of transition metal complexes incorporating a Schiff base derived from 2-aminophenol and 4-dimethoxyaminobenzaldehyde have been well documented [9-11]. The coordination compounds of lanthanum and cerium formed with 1-nitroso-2-naphthol and amino acids showed good antibacterial effectiveness [12,13]. The cerium metal chelates with piperazine-based Schiff base ligand exhibits potent antimicrobial and anticancer activity [14].

The present research explores the synthesis and spectroscopic analysis of cerium (III) mixed-ligand complexes containing a Schiff base derived from 2-aminophenol and 4-dimethylaminobenzaldehyde as primary coordinating ligand along with L-valine, L-phenylalanine, and L-isoleucine as secondary ligands. Their biological activities were also evaluated.



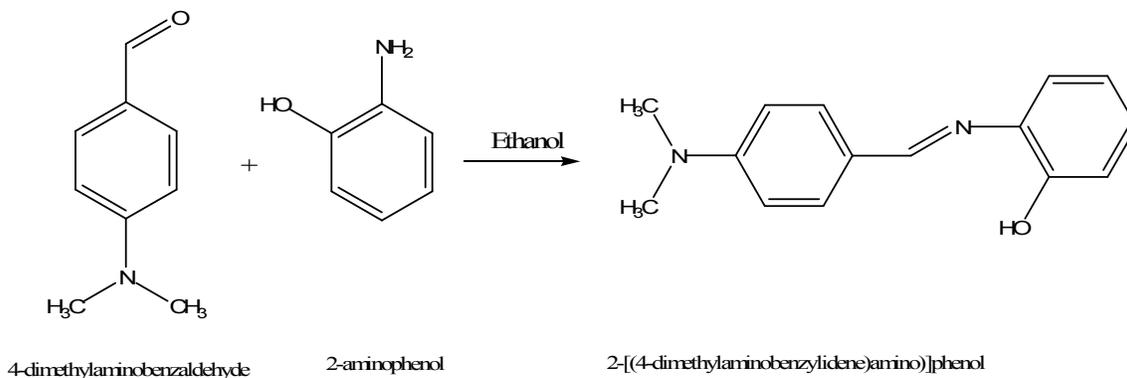
II. MATERIAL AND METHODS

The Analytical reagent grade cerium chloride heptahydrate, 4-dimethylamino benzaldehyde, 2-aminophenol and ligands *L*-valine, *L*-phenylalanine, *L*-isoleucine were used as such as obtained from S.D. Fine Chemicals. The solvents used in this study, including DMF, DMSO and ethyl alcohol were purified and distilled according to standard procedure.

The elemental composition (CHN) was determined with a Thermo Finnigan elemental analyser. Molar conductivity measurements were recorded using an Equiptronics auto ranging conductivity meter. Magnetic susceptibility was evaluated at room temperature by the Gouy method, employing $\text{Hg}[\text{Co}(\text{SCN})_4]$ as a reference compound. Infrared spectra were obtained in the $4000\text{--}400\text{ cm}^{-1}$ region using the KBr pellet method on an FT-IR spectrophotometer, while electronic absorption spectra were recorded with a Shimadzu UV-VIS 1800 spectrophotometer.

SYNTHESIS OF SCHIFF BASE

An equimolar mixture of 4-dimethylaminobenzaldehyde (1.49 g, 0.01 mol) and 2-aminophenol (1.09 g, 0.01 mol) was dissolved in 50 mL of ethanol. The resulting solution was refluxed in a boiling water bath and continuously stirred for 30 minutes. Formation of the Schiff base was indicated by the appearance of a yellow solid. The precipitated product was isolated by filtration, washed repeatedly with hot ethanol, and allowed to dry. Final purification was carried out by recrystallization using hot methanol, affording yellow crystalline solid. The synthesis of the Schiff base ligand is depicted in Scheme 1.



Scheme 1: Synthesis of Schiff base (DBAP) ligand

SYNTHESIS OF CERIUM COMPLEXES

The cerium complexes were synthesized using cerium (III) chloride heptahydrate, a Schiff base ligand, and selected amino acids, namely *L*-valine, *L*-phenylalanine, and *L*-isoleucine. An ethanolic solution of the Schiff base (20 cm³; 0.481 g, 0.002 M) was added gradually to an aqueous solution of cerium chloride heptahydrate (10 cm³; 0.372 g, 0.001 M) with continuous stirring. Subsequently, an aqueous solution of the corresponding amino acid (10 cm³; 0.001 M) was introduced into the mixture. The pH of the reaction medium was adjusted to approximately 8.5 by the slow addition of diluted ammonia solution. The reaction mixture was then refluxed for two hours and allowed to cool to ambient temperature. The radish brown precipitate formed was collected by filtration, washed thoroughly with ethanol, and dried under vacuum. The prepared cerium complexes were further characterized using physicochemical and spectroscopic techniques, and their antibacterial properties were evaluated.

ANTIBACTERIAL SCREENING

The synthesized Ce (III) complexes were evaluated for antibacterial activity using the Agar cup diffusion method against *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis* and *Shigella sonnei*. Sterile molten Muller Hinton



agar butt inoculated with the respective bacterial cultures was poured into sterile Petri plates and allowed to solidify. The wells of 8 mm diameter were prepared using sterile cork borer. The test solutions of concentration of 1mg/ml was prepared in DMF and inoculated into the wells with sterile pipette. The plates were incubated at 37°C for 24 hours. Antibacterial activity was determined by measuring the diameter of the zone of inhibition surrounding the well. Tetracycline was used as the reference standard for comparison of the antibacterial efficacy of the metal complexes.

III. RESULT AND DISCUSSION

The general reaction representing the formation of mixed-ligand cerium complexes is shown below.



Where, M = CeCl₃·7H₂O, HL = L-valine/ L-phenylalanine/ L-isoleucine, DBAP=Schiff base 2-[(4-(dimethyl amino)benzylidene amino)]phenol.

The cerium complexes were isolated as reddish-brown solids. All complexes exhibited partial solubility in DMF and DMSO aprotic solvents but complete insolubility in water and common organic solvents. The decomposition temperature of all compounds showed well-defined metal–ligand strong coordination frameworks, and their low molar conductance values verify their non-electrolytic behaviour. The results of CHN elemental analysis (Table 1) indicate the successful synthesis of mixed-ligand complexes possessing a 1:2:1 stoichiometric ratio of formula [M(DBAP)₂·(L)·2H₂O]. The physical properties of cerium complexes are summarized in Table 2.

TABLE 1 : ELEMENTAL ANALYSIS DATA OF CERIUM COMPLEXES

Sr. No.	Complex	Elemental Analysis (%)							
		Ce		N		H		C	
		Obs.	Cal.	Obs.	Cal.	Obs.	Cal.	Obs.	Cal.
1	[Ce(DBAP) ₂ ·(Val)2H ₂ O]	18.22	18.18	9.10	9.08	5.65	5.75	54.45	54.53
2	[Ce(DBAP) ₂ ·(Phe).2H ₂ O]	17.12	17.11	8.40	8.55	5.40	5.42	57.19	57.20
3	[Ce(DBAP) ₂ ·(Ileu)2H ₂ O]	17.83	17.85	8.90	8.92	5.93	5.91	55.11	55.09

TABLE 2: THE PHYSICAL DATA OF CERIUM COMPLEXES

Sr. No.	Complex	D.T./M. P (°C)	Color	Empirical Formula	Formula Weight (g)
1	[Ce(DBAP) ₂ ·(Val)2H ₂ O]	220	Reddish Brown	C ₃₅ H ₄₄ CeN ₅ O ₆	770.87
2	[Ce(DBAP) ₂ ·(Phe). 2H ₂ O]	240	Reddish Brown	C ₃₉ H ₄₄ CeN ₅ O ₆	818.91
3	[Ce(DBAP) ₂ ·(Ileu)2H ₂ O]	215	Reddish Brown	C ₃₆ H ₄₆ CeN ₅ O ₆	784.90

UV-VISIBLE SPECTROSCOPIC STUDY

UV-Visible spectral analysis of cerium complexes was carried out in DMF at a concentration of 10⁻³ M. The absorption data summarized in Table 3 indicate three main electronic transitions occurring between 268–279 nm, 341–350 nm, and 424–431 nm respectively. These transitions arise from π→π* and n→π* ligand-centred excitations as well as ligand-to-metal charge transfer interactions [15]. The UV-Visible spectrum of synthesized cerium complexes are represented in figure 1-3.

TABLE 3: UV-VISIBLE SPECTROSCOPIC DATA OF CERIUM COMPLEXES

Sr. No.	Complex	ν (cm ⁻¹)	λ(nm)	Assignments
1	[Ce(DBAP) ₂ ·(Val)2H ₂ O]	37313.43	268	π→π*
		29325.51	341	n→π*
		23201.86	431	L→M
2	[Ce(DBAP) ₂ ·(Phe). 2H ₂ O]	36231.88	276	π→π*
		29069.77	344	n→π*



		23255.81	430	L→M
3	[Ce(DBAP) ₂ .(Ileu)2H ₂ O]	35842.29	279	π→π*
		28571.42	350	n→π*
		23584.91	424	L→M

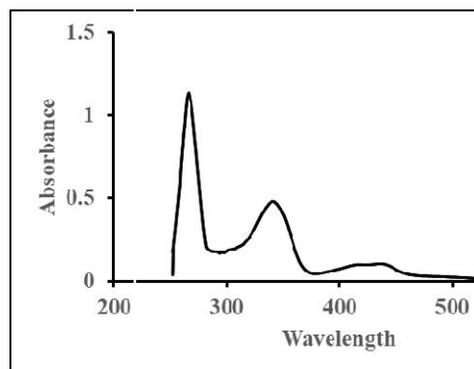


Figure 1: UV-visible spectrum of [Ce(DBAP)₂.(Val).2H₂O]

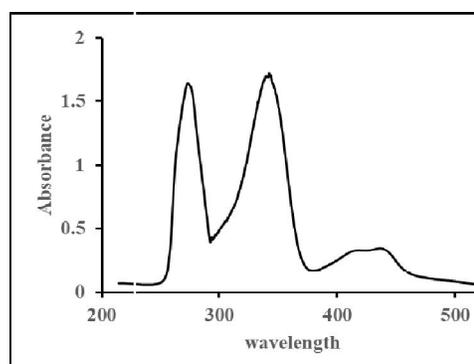


Figure 2: UV-visible spectrum of [Ce(DBAP)₂.(Phe).2H₂O]

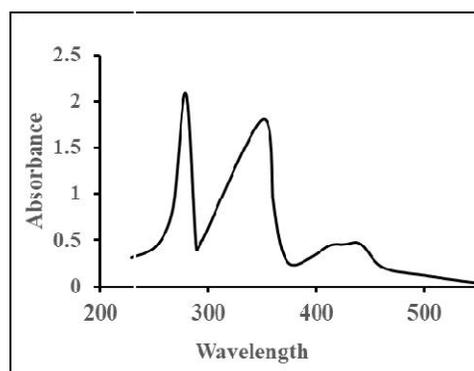


Figure 3: UV-visible spectrum of [Ce(DBAP)₂.(Ileu)2H₂O]



CONDUCTOMETRIC AND MAGNETIC SUSCEPTIBILITY INVESTIGATIONS

Molar conductivity measurements of synthesized Ce(III) complexes were carried out in DMF at 10^{-3} M concentration. The recorded conductance values between $0.130\text{--}0.270$ Mho $\text{cm}^2 \text{mol}^{-1}$ (Table-4) are significantly low, confirming the non-electrolytic nature of the complexes [16]. After applying diamagnetic corrections, magnetic susceptibility measurements yielded magnetic moment values in the range of $1.76\text{--}1.81$ BM for the cerium complexes (Table-4). These results demonstrate that the complexes possess paramagnetic character [17-18].

TABLE 4: ELECTRICAL CONDUCTANCE AND MAGNETIC RESPONSE DATA OF CERIUM COMPLEXES

Sr. No.	Complex	(Xm)	(Xg)	μ_{eff} (B.M.)	Λ_m (Mhos $\text{cm}^2 \text{mol}^{-1}$)
1	[Ce(DBAP) ₂ .(Val)2H ₂ O]	1.40×10^{-3}	1.81×10^{-6}	1.99	0.000130
2	[Ce(DBAP) ₂ .(Phe). 2H ₂ O]	1.29×10^{-3}	1.57×10^{-6}	1.93	0.000150
3	[Ce(DBAP) ₂ .(Ileu)2H ₂ O]	1.32×10^{-3}	1.69×10^{-6}	1.95	0.000270

FTIR SPECTROSCOPIC STUDY

The infrared spectra of the synthesized cerium mixed-ligand complexes are presented in Table 5. A broad band at $3415\text{--}3416$ cm^{-1} indicates the presence of coordinated water molecules [6]. In the free amino acids, bands at $2666\text{--}3030$ cm^{-1} and $3427\text{--}3448$ cm^{-1} correspond to COO^- and NH_2 stretching vibrations, respectively. Upon complexation, the COO^- band disappears, and the NH_2 band overlaps with the water absorption, indicating the participation of both groups in coordination [19]. The azomethine ($\text{HC}=\text{N}$) stretching at 1583 cm^{-1} shifts slightly to $1581\text{--}1587$ cm^{-1} in the complexes, confirming coordination through the nitrogen atom [19]. Furthermore, FT-IR spectrum of the free Schiff base ligand shows a phenolic O-H stretching band at 3342 cm^{-1} , which disappears in the cerium complexes suggesting the deprotonation and coordination of phenolic OH group to the cerium metal ion. New bands observed at $582\text{--}597$ cm^{-1} and $465\text{--}470$ cm^{-1} , absent in the free ligands, are assigned to M-O and M-N vibrations, supporting the involvement of oxygen and nitrogen atoms from the azomethine and hydroxyl groups in chelation. The FTIR spectrum of synthesized cerium (III) complexes and Schiff base are shown in figure 4-7.

TABLE 5: IR SPECTRAL DATA OF SYNTHESIZED CERIUM MIXED-LIGAND COMPLEXES

Sr. No.	Complex	FT-IR Peaks (cm^{-1})					
		ν O-H	ν COO A. A.	ν NH ₂ A. A.	ν C=N (SB)	ν M-N	ν M-O
1	Schiff base	3342	-	-	1583	-	-
2	L-Valine	-	2976 (B)	3430	-	-	-
3	L-Phenylalanine	-	3030 (B)	3448	-	-	-
4	L-Isoleucine	-	2966 (B)	3427	-	-	-
5	[Ce(DBAP) ₂ .(Val)2H ₂ O]	3416	-	-	1581	465	582
6	[Ce(DBAP) ₂ .(Phe). 2H ₂ O]	3416	-	-	1587	470	596
7	Ce(DBAP) ₂ .(Ileu)2H ₂ O]	3416	-	-	1587	465	597



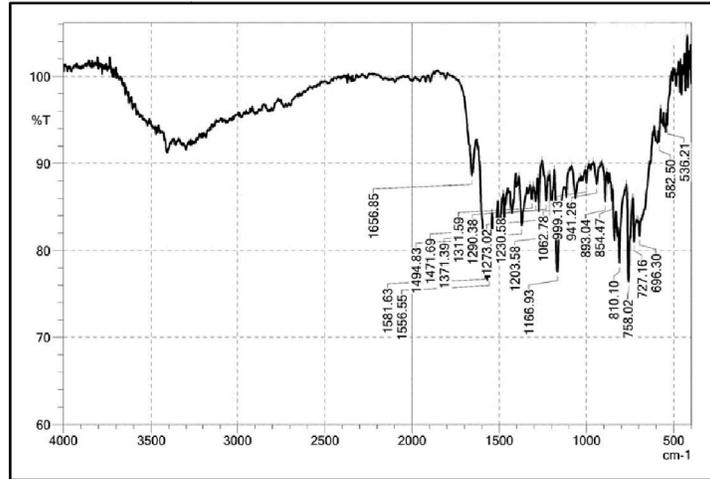


Figure 4: FTIR Spectra of [Ce(DBAP)₂(Val).2H₂O]

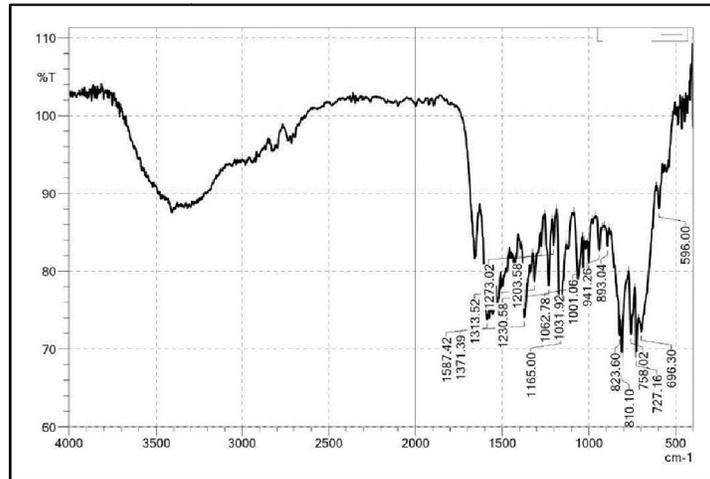


Figure 5: FTIR Spectra of [Ce(DBAP)₂(Phe).2H₂O]



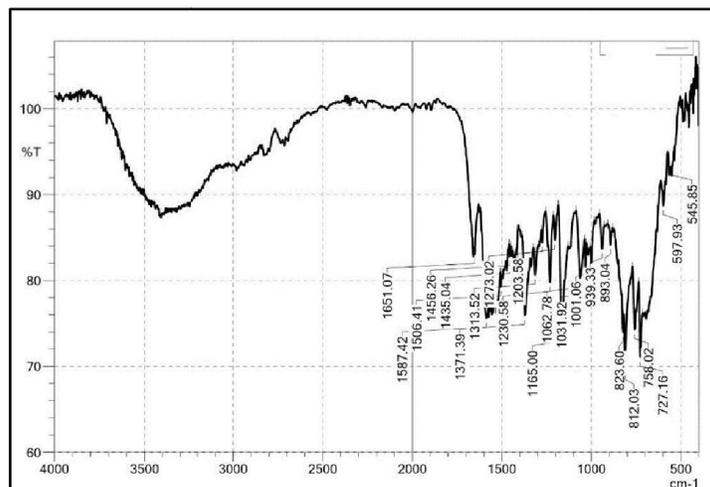


Figure 6: FTIR Spectra of [Ce(DBAP)₂(Ileu).2H₂O]

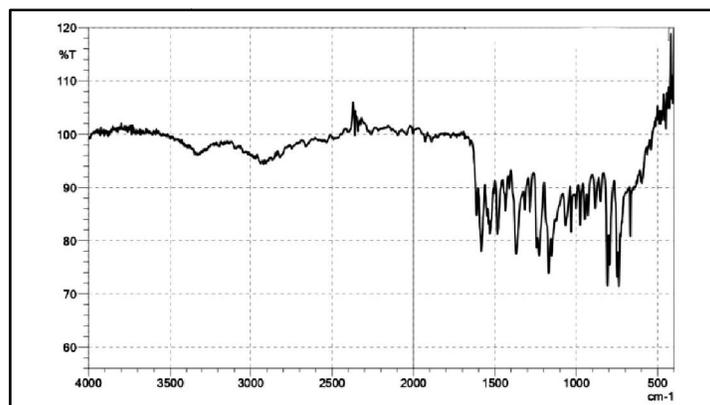


Figure 7: FTIR Spectra of Schiff base (DBAP)

ANTIBACTERIAL ACTIVITY

The antibacterial activity of the synthesized cerium (III) mixed-ligand complexes was investigated against two Gram-positive bacteria (*Staphylococcus aureus* and *Bacillus subtilis*) and two Gram-negative bacteria (*Escherichia coli* and *Shigella sonnei*). The results indicate that the complexes exhibit significant inhibitory effects against all tested microorganisms. The Zone of Inhibition of synthesized complexes of cerium (III) are depicted in Table-6 and figure 8. Among the studied strains, the complexes demonstrated comparatively stronger activity against *B. subtilis* and *E. coli*, while relatively lower inhibition was observed for *S. aureus* and *S. sonnei*. Such differences in antimicrobial ability of complex may arise due to structural variations in the bacterial cell membrane.

The improved antibacterial activity of the studied complexes may be attributed due to chelating effect which enhances the lipophilic nature of the complexes [20]. Increased lipophilicity facilitates penetration through the phospholipid membrane, allowing the complexes to interfere with essential biological processes of bacteria and ultimately causes inhibition of bacterial growth.



TABLE 6: ANTIMICROBIAL EFFECTIVENESS OF MIXED-LIGAND NEODYMIUM COMPLEXES (mm)

Sr. No.	Complexes	Zone of Inhibition in mm			
		<i>S. aureus</i>	<i>B. subtilis</i>	<i>E. Coli</i>	<i>S. sonnei</i>
1	[Ce(DBAP) ₂ (Val)2H ₂ O]	19	23	30	17
2	[Ce(DBAP) ₂ (Phe). 2H ₂ O]	20	24	25	19
3	Ce(DBAP) ₂ (Ileu)2H ₂ O]	20	25	23	20

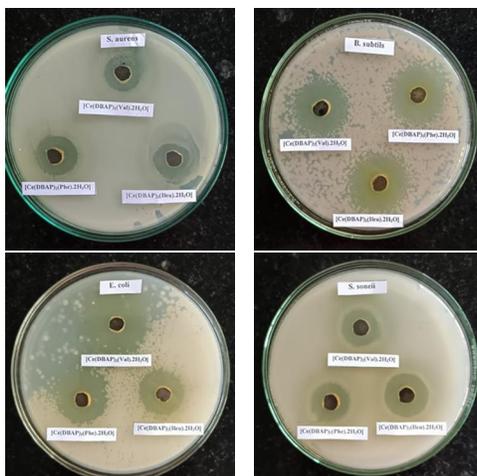


Figure 8: Zone of Inhibition of synthesized complexes of cerium (III)

The proposed structures of the cerium complexes, derived from physicochemical and spectral analyses, are depicted in Figures 9–11.

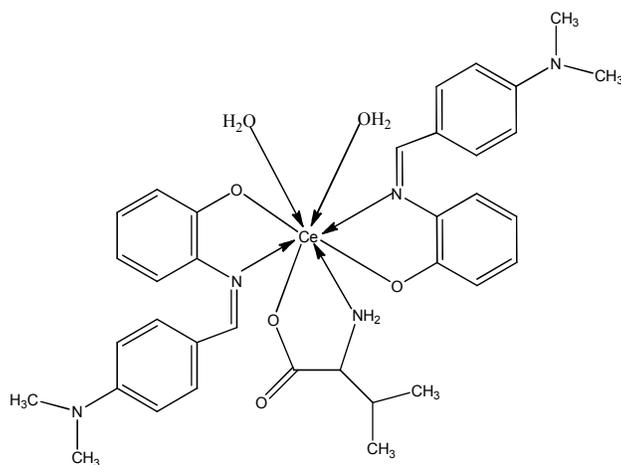


Figure 9: Proposed structure of [Ce(DBAP)₂(Val)·2H₂O]



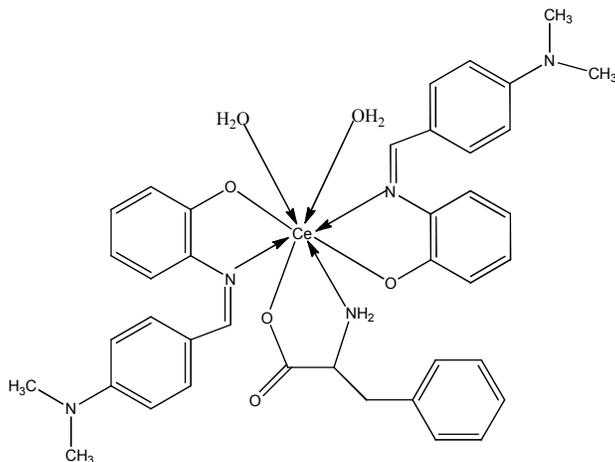


Figure 10: Proposed structure of $[Ce(DBAP)_2(Phe) \cdot 2H_2O]$

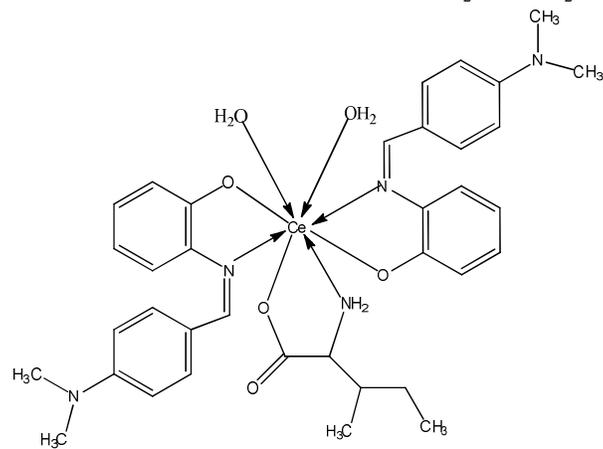


Figure 11: Proposed structure of $[Ce (DBAP)_2 (Ileu) \cdot 2H_2 O]$

IV. CONCLUSION

A series of mixed-ligand cerium (III) complexes were synthesized and systematically characterized. Conductivity studies reveal that the complexes behave as non-electrolytes. Based on the experimental observations, it can be inferred that the amino acid ligands coordinate to the metal ions in a bidentate fashion, involving the oxygen atom of the carboxylate (COO^-) group and the nitrogen atom of the amino (NH_2) group. In contrast, the Schiff base ligands coordinate through the oxygen atom of the hydroxyl (OH) group and the nitrogen atom of the azomethine ($C=N-H$) group. Overall, the findings confirm that all newly synthesized cerium complexes in this study display a coordination number of eight. Furthermore, the synthesized new Ce (III) complexes exhibit enhanced antibacterial activity compared to their respective free ligands and metal salts against the tested bacterial strains.

V. ACKNOWLEDGMENT

The Authors Uttam N. Dhaigude, Nikita U. Dhaigude & Kirti J. Mhatre are thankful to the Principal, Dr. Ganesh A. Thakur, Rayat Shikshan Sanstha's Mahatma Phule Arts, Science & Commerce College, Panvel for their encouragements and providing research facilities. Authors are also thankful to Mr. S. L. Gove, Mr. S. S. Avchite and Dr. P. B. Thakur for their valuable guidance.



REFERENCES

- [1]. Md. Ashrafuzzaman, F. K. Camellia, A Al Mahmud, Md. J. Pramanik, K. Nahar, Md. M. Haque and Md. Kudrat-E-Zahan, "Bioactive mixed ligand metal complexes of Cu (II), Ni (II), and Zn (II) ions: Synthesis, Characterization, Antimicrobial and Antioxidant Properties", *J. Chil. Chem. Soc.*, 66(3), 5295-5299, 2021.
- [2]. Eman A.M. Khalil and G. G. Mohamed, "Synthesis and characterization of some transition and inner transition mixed ligand complexes derived from Schiff base ligand and o-aminophenol", *Inorg. Chem. Commun.*, 153, 110825, July 2023.
- [3]. A R. Patil, K. J. Donde, S. S. Raut, V. R. Patil and R. S. Lokhande, "Synthesis, characterization and biological activity of mixed ligand Co (II) complexes of schiff base 2-amino-4-nitrophenol-n-salicylidene with some amino acids", *J. Chem. Pharm. Res.*, 4(2), 1413-1425, 2012.
- [4]. S. P. Sridevi, C. R. Girija and C. D. Satish, "Synthesis, structure and reactivity of schiff base transition metal mixed ligand complexes derived from Isatin and Salal", *Orient. J. Chem.*, 37(1), 169-176, 2021.
- [5]. Z. A. Taha, A. K. Hijazi and W.M. Al Momani, "Lanthanide complexes of the tridentate Schiff base ligand salicylaldehyde-2- picolinoylhydrazone: Synthesis, characterization, photophysical properties, biological activities and catalytic oxidation of aniline", *J. Mol. Struct.*, 1220, 128712, Nov.2020.
- [6]. K. Andiappan, A. Sanmgam, E. Deivanayagam, K. Karuppasamy, Hyun-Seok Kim and D. Vilraman, "In vitro cytotoxicity activity of novel Schiff base ligand-lanthanide complexes", *Nature*, 8(1), 3054, Feb. 2018.
- [7]. N. P. Ebosie, "Synthesis, Characterization, molecular docking, and computational study of schiff base ligand derived from 4-aminoantiprine and 2-aminophenol and its Nd (III), Sm (III), Gd (III) and Dy (III) complexes", *J. Chem. Soc. Nigeria*, 50(2), 373-388, 2025.
- [8]. N. P. Yahaya and M. S. Mukhtar, "Synthesis, Characterization and Antibacterial Activity of Schiff Base and its Metal (II) Complexes Derived From 3-Aminophenol and Benzaldehyde", *IJRSI*, 7(10), 2321-2705, 2020.
- [9]. A A. Maihub, F. S. Alassbaly, M. Mailoud El-Ajaily and A. M. Etorki, "Modification on synthesis of mixed ligand chelates by using Di- and Trivalent transition metal ions with Schiff base as primary ligand", *GSC*, 4, 103-110, (2014).
- [10]. M. M. El-ajaily, F. S. Alassbaly, A. M. Etorki and A. A. Maihub, "Mixed-Ligand chelate formation of Co(II), Ni(II), Cu(II) and Zn(II) ions with Schiff base as Main ligand and amino acid as Co-ligand", *Int. Res. J. Pure Appl. Chem.*, 5(3), 229-237, 2015.
- [11]. F. S. Alassbaly, A. A. Maihub, S. F. Ben-Gweirif, M. M. El-ajaily and T. H. Al-Noor, "Chelation Trends and Antibacterial Activity of Some Mixed Ligand Chelates", *Saudi J. Pathol. Microbiol.*, 1(2), 29-35, 2016.
- [12]. G. A. Thakur, U. N. Dhaigude And S. S. Patil, "Some mixed ligand complexes of Lanthanum (III) Using 1-Nitroso-2-naphthol and amino acids", *Asian J. Chem.*, 30(7), 1585-1589, 2018.
- [13]. G. A. Thakur, U. N. Dhaigude and P. B. Thakur, "Synthesis, Spectral Characterization and Antibacterial Studies of Mixed Ligand La (III) and Ce (III) Complexes Derived From 1-nitroso-2-naphthol and Some Amino Acids", *Orient. J. Chem.*, 36(4), 632-639, 2020.
- [14]. V. Geethalakshmi, N. Nalini, S.S. Sabithamala, D. Tamilselvi, and C.T. Theivarasu, "Synthesis and spectral studies of Piprazine Schiff Base Lanthanide (III) complexes and their microbial and anticancer activity, *Asian J. Chem.*, 34(1), 155-161, 2022.
- [15]. F. Y. Larial, M. M.El-ajaily, N. M. El-Barasi, A. A. Maihub, R. K. Mohapatra and T. H. Al-Noor, "Synthesis and Spectral Studies of Mixed Ligand Complexes of Trivalent Metal Ions", *ARPG*, 7(1), 1-9, 2022.
- [16]. J. M. Pawara, V. S. Kamble, S. S. Kamble, D. Y. Patil, H. P. Deokar and D. K. Patil, "Preparation of mixed ligand complexes of Cerium (III) metal using multidentate ligands and investigation of their physicochemical, Spectral, Thermal, and Antibacterial Properties", *J. Adv. Zool.*, 44(8), 123-132, 2023.



- [17]. D. Patil, J. Pawara, B. Patil and V. Kamble, "Antibacterial detection of some synthesized Cerium (III) metal mixed ligand complexes along with their physicochemical, spectral and thermal study", *Shodhasamhita: J. Fundam. Comp. Res.*, 9(6), 76-89, 2022.
- [18]. G. A. Thakur, U. N. Dhaigude1 and P.V. Bhise, "Studies on Some Mixed Ligand Ternary Complexes of Cerium (III) Employing 1-Nitroso-2-naphthol and Amino Acids", *Asian J. Chem.*, 30(11), 2467-2471, 2018.
- [19]. F. S. Alassbaly, M. M. El-Ajaily, S. F. Ben-Gweirif and A. Ali Maihub, "Preparation, Spectroscopic Investigation and Biological Activity of New Mixed Ligand Chelates", *J. Chem. Soc. Pak.*, 36(6), 1034-1042, 2014.
- [20]. E. M. Jincy, P. K. Rejimon and M. K. Muraleedharan Nair, "Synthesis, characterization and antimicrobial studies of some lanthanide (III) complexes with a tridentate ono donor Schiff base ligand", *IJAASR*, 2(2), 246-251, 2017.

