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Synthesis, Physical and Spectral Investigations and Biological Studies of Mixed Lig and Lanthanum Complexes

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ABSTRACT

In the present study the synthesis of mixed ligand lanthanum complexes has been carried out by using (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol as a primary ligand and various amino acids such as L-proline, L-valine and L-serine as secondary ligands. Different physico-chemical methods viz. elemental analysis, magnetic susceptibility measurements and complexometric estimation; spectroscopic methods viz. UV-Visible, IR and XRD and thermal analysis were used for characterization of lanthanum complexes. Elemental analysis and complexometric estimation confirm the contents of metal and elements (C, H, N) in synthesized lanthanum complexes. The non-electrolytic and diamagnetic properties of the complexes are revealed by conductometric method and room temperature magnetic susceptibility technique respectively. The transition of the electrons during formation of complexes is revealed by the study of electronic absorption spectra. The functional groups present in complexes are concludedby FTIR spectra. Water molecules and moieties of primary and secondary ligands are confirmed by thermal and XRD analysis. The anti-bacterial study of the lanthanum complexes has been carried out by tube dilution and agar cup methods.

Keywords: Lanthanum complexes, spectral investigation and biological study.

INTRODUCTION

Several types of research showed the role of mixed ligand complexes in different biological systems(1, 2). Many metal complexes are studied for activation of enzyme in biological processes (3).Inter-relation of stability of mixed ligand complexes and their anti-microbial activity has been also studied (4).Some researchers have reported anti-cancer and anti-tumor activities of metal complexes (5, 6). N- and O-donor ligands have been used for synthesis of metal complexes to study various anti-microbial and anti-fungal activities (7-9).The complexes with (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol have been characterized (10). Numerous researchers have reported the anti-diabetic, anti-bacterial and anti-fungal activities of many mixed ligand complexes with amino acids (11-13).Transition metal complexes have been synthesized and studied for various biological activities (14-15). Many complexes have been derived from Lanthanide and Actinide metal ions and studied for biological activities (16-17).

With regard to the literature study, the authors have decided to synthesize, characterize and study biological activity of mixed ligand lanthanum complexes. Cupron i.e. (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol was used as a primary ligand and L-proline, L-valine and L-serine were used as secondary ligands for synthesis of lanthanum complexes. Elemental analysis, complexometric estimation, conductometry, room temperature magnetic susceptibility measurements, UV-Visible spectroscopy, FTIR spectroscopy, thermal methods and XRD techniques were used for characterization for all synthesized lanthanum complexes.

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EXPERIMENTAL

1. Materials

The chemicals and solvents used for laboratory work were of analytical grade. Lanthanum chloride heptahydrate, cupron and amino acids *viz.* L-proline, L-valine and L-serine used for synthesis were from E. Merck. Distilled and purified solvents *viz.* ethanol, DMF and DMSO were used whenever necessary. Standard protocol was followed for distillation and purification of the solvents (18-20).

2. Synthesis of Complexes

The metal salt (Lanthanum chloride heptahydrate), cupron [(2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol] and amino acids (L-proline, L-valine and L-serine) were used in 1:2:1 proportion for the synthesis of mixed ligand lanthanum complexes. 10 cm^3 aqueous solution of lanthanum(III) chloride heptahydrate (371 mg, 1mmol) is mixed with 10 cm^3 of ethanolic solution of (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol (454 mg, 2mmol). The reaction mixture was stirred in boiling water bath. After stirring, an aqueous solution (10 cm^3) of amino acid (1 mmol) was added with stirring to the hot mixture of lanthanum(III) chloride heptahydrate and (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol. The resultant mixture was again stirred and heated. The pH of the resultant mixture was raised by adding diluted ammonia solution to precipitate the complex. The synthesized complex was cooled. The complex was filtered by using Buckner funnel and washed with aqueous alcohol. The drying of synthesized complex was carried out under vacuum. All synthesized complexes were further used for spectral investigation and anti-microbial activities.

3. Instrumentation

The Thermo Finnigan Elemental Analyzer at Department of Chemistry, I.I.T., Mumbai was used for elemental analysis. The complexometric estimation was used to measure metal content in the complexes (21, 22). The 10^{-3} molar solutions of metal complexes in DMF were used to measure their molar conductance. The conductance measurements were carried out on Equip-tronics Conductivity Meter. The Guoy's method was used to measure magnetic susceptibility of the complexes. The $Hg[Co(SCN)_4]$ was used as a calibrant for the magnetic study. The 10^{-4} molar solutions of metal complexes in DMF were used to study electronic absorption spectra in ultra-violet region. The electronic absorption spectra were obtained from Shimadzu Spectrophotometer.The FTIR spectra of all synthesized complexes were recorded on Shimadzu Spectrophotometer. The KBr disc was used to obtain the FTIR spectra in the region 4000-400 cm^{-1}. The complexes were studied for thermal analysis at Department of Chemistry, I.I.T. Mumbai. The study was carried out on Perkin-Elmer Diamond TG-DTA Instrument. The TG and DTA were obtained by observing the change in weight of the complexes with increasing temperature. The temperature was increased upto 900^{o}C and the heating rate was 10^{o}C per minute.

4. Antibacterial Study

4.1 Tube dilution method

To see the potential of the complex as an antimicrobial agent, the minimum inhibitory concentration was found out by tube dilution method against the selected bacterial strains *Staphylococcus aureus*, *Corynebacteriumdiphtheriae*, *Salmonella typhi*and *Pseudomonas aeruginosa* using Mueller Hinton broth as the culture medium.

The stock solution of test sample was prepared by dissolving 10 mg of test compound in 10 cm^3 DMSO. The aliquots of 10, 20, 30, 40, ……,300 µg/cm^3 were prepared from the stock using sterile broth. The bacterial inoculums of several species (*S. aureus*, *C. diphtheriae*, *S. typhi*and *P. aeruginosa)* were prepared in sterile Mueller Hinton broth and adjusted so as to get 10^6 cm^{-3} bacteria. The 5 cm^3 of each aliquot was taken in a sterile borosilicate tube (150 x 20 mm) and inoculated with 0.1 cm^3 inoculum aseptically. The tubes were kept for incubation at 37^{o}C for24 hrs.and then observed for the growth of the

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microorganisms. The minimum concentration, at which the growth was absent, was considered as Minimum Inhibitory Concentration (MIC).

A positive control was maintained containing 5 cm^3 broth and 0.1 cm^3 respective inoculums while tetracycline was taken as negative control at the concentration of 300 µg/cm^3diluted with broth.

4.2 Agar cup method

The inhibition zone was estimated to check the potential of the test samples against the different species of bacteria (*S. aureus*, *C. diphtheriae*, *S. typhi*and *P. aeruginosa).* The nutrient agar inoculated separately with the desired strains was poured upto the depth of 5 mm, in the sterile plates and allowed to solidify. Three wells of 8 mm diameter each, was punched into an agar to make wells. In one cup, test sample of 0.001M was filled where the other well were used for DMSO (1:1 v/v) and standard control (Tetracycline) respectively. The plates were kept in refrigerator for 10 min. for diffusion in the surrounding medium and then incubated at 37^oC for 24 hrs. The zone of inhibition by each sample as well as DMSO and standard was measured in mm from the edge of the cup.

RESULTS AND DISCUSSION

1. Synthesis

All metal complexes were synthesized using lanthanum chloride heptahydrate, (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol as a primary ligand and L-proline, L-valine and L-serine as secondary ligands in 1:2:1 proportion. The reaction is-

$$LaCl_3 \cdot 7H_2O + 2HCup + HL \longrightarrow [La(Cup)_2(L) \cdot 2H_2O] + 3HCl + 5H_2O$$

Where,

HCup: (2Z)-2-(N-hydroxyimino)-1,2-diphenylethan-1-ol [i.e. Cupron]

HL: Amino acid

2. Physico-Chemical Properties

2.1 Colour

The colour of all synthesized complexes is white. (Table No.: 1)

2.2 Hygroscopic Property and Thermal Stability

All synthesized complexes are non-hygroscopic in nature. The decomposition temperature of all complexes is in the range of 245-260^oC. The high decomposition temperature indicates there is strong bond between metal and ligands. (Table No.: 2)

2.3 Solubility

All synthesized complexes are found insoluble in solvents like ethanol, acetone, etc. They are partially soluble in DMF and DMSO.

2.4 Conductance

The molar conductance of the complexes was measured by preparing 10^{-3} M solution of synthesized complexes in DMF. The molar conductance was found in the range of 0.0010-0.0013 mhos cm^2 mol^{-1}. The range of the molar conductance indicates the non-electrolytic nature of synthesized complexes (23). (Table No.: 3)

2.5 Elemental Analysis

The data of elemental analysis is mentioned in Table 3. The data of elemental analysis concludes the general formula of the synthesized complex, 1:2:1. (Table No.: 3)

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2.6 Magnetic Properties

Diamagnetic corrections were employed to calculate magnetic susceptibility of synthesized lanthanum complexes. These magnetic values are mentioned in Table 4 which indicates the diamagnetic nature of lanthanum complexes (24).(Table No.: 4)

3. Electronic Absorption Spectra

The 10^{-4} M solutions of metal complexes were prepared in DMF to study their electronic absorption spectra. The data showed three transition ranges, 272-279 nm (36765-35842 cm^{-1}), 331-337 nm (30211-29674 cm^{-1}) and 387-392 nm (25840-25510 cm^{-1}). The transition range 272-279 nm is indicates $\pi \rightarrow \pi^*$ transition, 331-337 nm indicates $n \rightarrow \pi^*$ and 387-392 nm indicates charge transfer transitions from ligands to the metal.(Table No.: 5)

4. Infra-red Spectra

FTIR spectra of all synthesized complexes were obtained over the range of 4000-400 cm^{-1}. All these spectra were taken from FTIR spectrometer using KBr discs.The FTIR spectrum does not show the band at ~3440 cm^{-1}. This indicates the formation of complex by deprotonation of hydroxyl group of cupron moiety. The band observed at 1100 cm^{-1} for C-O stretching of free cupron is shifted to lower wave number in the range of 1000-1015 cm^{-1} also indicates the formation of complex by deprotonation of hydroxyl group of cupron moiety. The ν (C=N) mode observed at 1650 $cm^{-1}$for free cupronis shifted to the range of 1480-1505 cm^{-1} indicates oxime nitrogen coordinated with metal. The band obtained in the range of 3270-3295 cm^{-1} concludes the presence of free oxime –OH group in cupron moiety. In plane and out of plane deformation mode shown by free cupron at ~780 cm^{-1} are shifted to higher wave number range 815-820 cm^{-1} indicates coordination of nitrogen atom of cupron with lanthanum metal ion. The band observed at ~3050 cm^{-1} and ~2960 cm^{-1} assigned for N-H asymmetric and N-H symmetric in free amino acid are shifted to higher wave number range 3130-3140 cm^{-1} and 2990-2998 cm^{-1} respectively. This shifting indicates coordination of nitrogen of amino acid with metal ion. The band observed at ~1595 cm^{-1} in free amino acid assigned for $\nu_{asymmetric}$(COO-) is shifted to higher wave number range 1610-1625 cm^{-1}. Also the band observed at ~1410 cm^{-1}in free amino acid assigned for $\nu_{symmetric}$(COO-) is shifted to lower wave number range 1375-1382 cm^{-1}. This shifting indicates the coordination of carboxylic acid group with metal ion through oxygen. Broad band is observed in the range of 3270-3350 cm^{-1} and a weak band observed in the range of 1575-1590 cm^{-1}. The broad band confirmed asymmetric and symmetric O-H stretching and the weak band confirmed H-O-H bending vibration. All these bands confirmed presence of coordinated water molecules in the complexes. Some weak bands observed at 400 $cm^{-1}$and 610 cm^{-1}. The weak band in the range of 400-408 cm^{-1} confirmed M-N vibration, where M is metal ion. Another weak band in the range of 610-615 cm^{-1} confirmed the M-O vibration in the complexes. All these frequencies indicate bonding between metal ion and oxygen of ligands and coordination between metal ion and nitrogen of ligands (25-27). (Table No.: 6)

5. Thermal Studies

Thermal study of mixed ligand complexes has been carried out in controlled nitrogen atmosphere. The complexes were heated at constant heating rate of 10°C/min. upto 900°C. All the three synthesized complexes show same behaviour of TG-DTA curves. There is gradual loss in weight due to decomposition of water molecules and ligand moieties with increasing temperature. The loss in weight obtained in the temperature range 130-174°C is due to loss of two coordinated water molecules. The loss in weight obtained in the temperature range 251-408°C is due to loss of amino acid moiety from the complex. The loss in weight obtained in the temperature range 632-835°C is due to loss of two molecules

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of cupron moiety. The constant plateau in TG after 835^{o}C shows completion of the decomposition reaction. The final product of decomposition reaction is metal powder. The metal powder converted to its oxides spontaneously in presence of trace oxygen in the nitrogen gas used for the study. The formation of metal oxide is also confirmed from XRD (24). (Table No.: 7)

6. Biological Studies

6.1 Tube dilution method

Four bacterial strains namely *S. aureus*, *C. diptheriae*, *S. Typhi*and *P. Aerruginosa* were screened against the complexes. The complexes were found more effective than metal salt, $LaCl_3.7H_2O$ and ligand, Cupron. The minimum inhibitory concentration ranged between 70-120 µg/cm^3(Table No.: 8 and 9). The MIC against positive bacteria was between 70 and 80 µg/cm^{3}where as for negative bacteria, it ranged between 100-120 µg/cm^3. It indicates the efficiency of complexes against gram positive strains (28). However, the efficiency of complexes against bacteria is very low as compared to the standard tetracycline. (Table No.: 8-9)

6.2 Agar cup method

The zone of inhibition was seen in all the three complexes. The complexes were more effective against positive strains than negative strains. The zone of inhibition shown by the complexes was less as compared to standard tetracycline.(Table No.: 10)

CONCLUSIONS

From the analysis of all results following conclusions can be drawn.

1. The decomposition temperature of the metal complexes is high which indicates formation of strong bond between metal and ligands.
2. Electrical conductance studies reveal non-electrolytic nature of the complexes.
3. Magnetic susceptibility data conclude diamagnetic behaviour of the complexes.
4. Electronic absorption spectra show intra ligand and charge transfer transition between ligands and metal.
5. FTIR spectral study concludes the bonding of metal ion with ligands.
6. Thermal studies explained the thermal behaviour of complexes on increasing temperature which confirmed presence of co-ordinated water molecules and ligand moieties in the complexes.
7. The antibacterial study reveals that the complexes are more active against *S. aureus*, *C. diptheriae*than *S. Typhi*and *P. Aerruginosa.*

On the basis above the coordination number 8 may be proposed for all the complexes. The structures of the complexes are mentioned in figure 1-3.

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Figure 1: Proposed Structure of [$La(Cup)_2(Pro).2H_2O$]

Figure 2: Proposed Structure of [$La(Cup)_2(Val).2H_2O$]

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Figure 3: Proposed Structure of $[La(Cup)_2(Ser).2H_2O]$

Table 1: Empirical Formula, Molecular Weight and Colour

Complex	Empirical Formula	Molecular Weight	Colour
$[La(Cup)_2(Pro)\cdot 2H_2O]$	$C_{33}H_{36}LaN_3O_8$	741.56	White
$[La(Cup)_2(Val)\cdot 2H_2O]$	$C_{33}H_{38}LaN_3O_8$	743.57	White
$[La(Cup)_2(Ser)\cdot 2H_2O]$	$C_{31}H_{34}LaN_3O_9$	731.52	White

Table 2: Decomposition Temperature and pH

Complex	Decomposition Temperature (^oC)	pH
$[La(Cup)_2(Pro)\cdot 2H_2O]$	245	7.00
$[La(Cup)_2(Val)\cdot 2H_2O]$	260	7.01
$[La(Cup)_2(Ser)\cdot 2H_2O]$	255	7.01

Table 3: Elemental Analysis and Molar Conductance Data

Complex	Elemental Analysis Found (Calculated)				Molar Conductance
	% M	*% C*	*% H*	*% N*	
$[La(Cup)_2(Pro)\cdot 2H_2O]$	18.76 (18.73)	53.49 (53.44)	4.94 (4.90)	5.68 (5.66)	0.0010
$[La(Cup)_2(Val)\cdot 2H_2O]$	18.68 (18.68)	53.33 (53.30)	5.18 (5.16)	5.68 (5.65)	0.0011
$[La(Cup)_2(Ser)\cdot 2H_2O]$	18.99 (18.99)	50.95 (50.90)	4.69 (4.68)	5.75 (5.74)	0.0013

Table 4: Magnetic Susceptibility Data (- 10^{-6} c.g.s. units)

Complex	X_g	X_m	μ_{eff}
$[La(Cup)_2(Pro)\cdot 2H_2O]$	-1.03×10^{-6}	-7.64×10^{-4}	Diamagnetic
$[La(Cup)_2(Val)\cdot 2H_2O]$	-1.04×10^{-6}	-7.75×10^{-4}	Diamagnetic
$[La(Cup)_2(Ser)\cdot 2H_2O]$	-1.00×10^{-6}	-7.33×10^{-4}	Diamagnetic

Table 5: Data of Electronic Absorption Spectra

Sr. No.	Complex	λ (nm)	ν (cm^{-1})	Proposed Assignments
1	$[La(Cup)_2(Pro)\cdot 2H_2O]$	279	35842	$\pi\rightarrow\pi^*$
		331	30211	$n\rightarrow\pi^*$
		392	25510	Charge-transfer
2	$[La(Cup)_2(Val)\cdot 2H_2O]$	275	36364	$\pi\rightarrow\pi^*$
		337	29674	$n\rightarrow\pi^*$
		392	25510	Charge-transfer
3	$[La(Cup)_2(Ser)\cdot 2H_2O]$	272	36765	$\pi\rightarrow\pi^*$
		332	30120	$n\rightarrow\pi^*$
		387	25840	Charge-transfer

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Table 6: FTIR Data

Sr. No.	Complex	ν (C-O) (Cup)	ν (C=N) (Cup)	ν (-OH) (Oxime) (Cup)	ν (M-N) (Cup)	ν (N-H) (Asym) (A.a.)	ν (N-H) (Sym) (A.a.)	ν (COO-) (Asym) (A.a.)	ν (COO-) (Sym) (A.a.)	ν (HOH) (Asym) (HOH)	ν (HOH) (Sym) (HOH)	ν (M-N) (Complex)	ν (M-O) (Complex)
1.	$[La(Cup)_2(Pro)\cdot 2H_2O]$	1000 (s)	1480 (w)	3270 (m)	815 (w)	3130 (w)	2990 (w)	1610 (s)	1375 (w)	3270 (m)	1575 (w)	400 (m)	610 (w)
2.	$[La(Cup)_2(Val)\cdot 2H_2O]$	1015 (s)	1505 (w)	3290 (m)	825 (w)	3137 (w)	2998 (w)	1620 (s)	1382 (w)	3350 (m)	1585 (w)	405 (m)	612 (w)
3.	$[La(Cup)_2(Ser)\cdot 2H_2O]$	1010 (s)	1500 (w)	3295 (m)	820 (w)	3140 (w)	2992 (w)	1625 (s)	1380 (w)	3310 (m)	1590 (w)	408 (m)	615 (w)

Table 7: Thermal Data

Sr. No.	Complex	Temperature Range (^oC)	Weight Loss Due to Loss of	% Weight Loss	
				Found	Calculated
1.	$[La(Cup)_2(Pro)\cdot 2H_2O]$	130-170	Two water molecules	4.90	4.86
		251-408	Amino acid	15.41	15.39
		635-820	Two cupron molecules	61.07	61.02
2.	$[La(Cup)_2(Val)\cdot 2H_2O]$	131-174	Two water molecules	4.88	4.85
		254-407	Amino acid	15.65	15.62
		632-825	Two cupron molecules	60.89	60.86
3.	$[La(Cup)_2(Ser)\cdot 2H_2O]$	138-173	Two water molecules	4.99	4.93
		252-402	Amino acid	14.29	14.23
		639-835	Two cupron molecules	61.27	61.26

Table 8: Data of Antibacterial Activity by Tube Dilution Method

Sr. No.	Complex	MIC (µg/cm^3)			
		S. aureus	***C. diphtheriae***	***S. typhi***	***P. aeruginosa***
1.	$[La(Cup)_2(Pro)\cdot 2H_2O]$	70	70	100	120
2.	$[La(Cup)_2(Val)\cdot 2H_2O]$	70	80	100	120
3.	$[La(Cup)_2(Ser)\cdot 2H_2O]$	80	70	120	110

Table 9: MIC of Metal Salts, Ligand and Tetracycline by Tube Dilution Method

Salt / Ligand / Tetracycline	MIC (µg/cm^3)			
	S. aureus	***C. diphtheriae***	***S. typhi***	***P. aeruginosa***
$LaCl_3.7H_2O$	100	150	150	200
Cupron	110	200	160	140
Tetracycline	1.5	2.0	1.5	8.0

Table 10: Antibacterial Activity (mm) by Agar Cup Method

Sr. No.	Complex	Antibacterial Activity (mm) with			
		S. aureus	***C. diphtheriae***	***S. typhi***	***P. aeruginosa***
1.	$[La(Cup)_2(Pro)\cdot 2H_2O]$	17	18	15	14
2.	$[La(Cup)_2(Val)\cdot 2H_2O]$	18	16	16	14
3.	$[La(Cup)_2(Ser)\cdot 2H_2O]$	15	18	14	15
4.	Tetracycline	30	25	26	18

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