



## Synthesis and Characterization of Neodymium(III) Ternary Complex Using Lansoprazole and Uracil as Ligands

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Ternary complex of neodymium has been synthesized by reacting neodymium(III) nitrate hexahydrate with two different (dual) biochemical ligands. One of the ligand used is an antiulcer drug, lansoprazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)pyridine-2-yl]methyl]sulfinyl]-1*H*-benzimidazole, other is uracil which is a RNA bases. The complex was synthesized in ethanolic medium and refluxed in reaction medium in 1:1:1, M:L:L ratio. The percentage yield of synthesized neodymium complex was 93 %. The complex was purple coloured solid and of the type ( $L_{\text{lanso}}.Nd.L_{\text{Ura}}.4H_2O$ ) $X.nH_2O$ , where  $X$  is  $NO_4^{2-}$ . The synthesized complex was characterized by various complementary techniques namely elemental analysis, Fourier transform infrared spectroscopy, nuclear magnetic resonance spectroscopy ( $^1H$  NMR), ultra violet-visible spectroscopy, mass spectroscopy, X-ray diffraction, scanning electron microscopy. An IR spectrum indicates that all the ligands behave as bidentate ligand. Molar conductance studies indicate electrolytic behaviour of the complex. Free energy changes were also calculated of synthesized complex. The complex has been screened for their antibacterial activity towards *Streptococcus faecalis* bacteria. The results revealed that the metal chelates showed more resistance as compared with parent drug.

**Keywords:** Neodymium, Spectroscopy, Lansoprazole, Uracil, Antibacterial activity.

### INTRODUCTION

Lanthanide metals are known to form coordination compounds with variable coordination number ranging from 3 to 12, which make them excellent spacers in assembling fascinating metal organic frameworks. In recent years, lanthanide complexes has attracted great attention among scientific community due their unique physico-chemical, structural and catalytic properties. They have various applications as functional materials, such as chem- and bio-sensors [1,2], electroluminescence [3-5], magnetic [6,7], laser materials and in diagnostic pharmaceutical [8-13]. Complexes play an important role in biological process in which enzymes are known to be activated by metal ions. They have been found to exhibit anticancer and antifungicidal properties also [14].

Similar to all other lanthanide metals, the contraction property of neodymium due to its 4*f* orbitals which are shielded by the 5*s* and 5*p* shells has direct impact on its physical and chemical properties. Attempts have been made for the synthesis and characterization of neodymium complexes [15-19]. Here we report a process for the synthesis of neodymium complex using two different biochemical ligands. One of the biochemical ligand is lansoprazole with chemical name 2-[[[3-

methyl-4-(2,2,2-trifluoroethoxy)pyridine-2-yl]methyl]sulfinyl]-1*H*-benzimidazole. It is a proton pump inhibitor and an antiulcer drug [20-23]. As the interaction of metal ions with nucleobases is of great interest because of their relevance to the essential, medical or toxic bioactivity of metal, where nucleobase molecule can coordinate as exogenous ligands in metalloproteins, function as cofactors in the enzymatic systems. Thus, the RNA base namely uracil is used as another biochemical ligand for the synthesis of neodymium ternary complex. The uracil is 2-oxy-4-oxy pyrimidine [24-27]. It posses the N- and O- donor atoms. The elemental analysis, FTIR,  $^1H$  NMR, UV spectra, mass spectra, XRD, SEM data of synthesized neodymium ternary complex is reported.

### EXPERIMENTAL

Neodymium(III) nitrate hexahydrate and uracil were procured from Rankem and ethylene glycol was procured from Merck. Lansoprazole was obtained from Nosh Lab Pvt. Hyderabad. All the chemicals were used as such without further purification. Spectroscopic grade solvents were employed for recording the spectra.

Conductance measurement was done in DMF. The melting point was recorded on Labotech instrument. FTIR spectra were

taken using Bruker Alpha Fourier transform infrared spectrometer to determine the functional group present in the samples between 4000-400  $\text{cm}^{-1}$ . The  $^1\text{H}$  NMR spectrum was recorded on Bruker DRX-300. Ellico, SL191 double beam UV-visible spectrophotometer was used for recording UV-visible spectra. The mass spectrum was studied on a Jeol SX-102 spectrometer using argon as the FAB gas. X-ray diffraction pattern was obtained using D8 advance X-ray diffractometer using  $\text{CuK}\alpha$  radiation to identify different phases. The X-ray diffraction intensity was recorded as a function of Bragg's  $2\theta$  in the angular range of  $5\text{--}70^\circ$ . Scanning electron microscope (SEM), model NOVA NANOSEM-430 of COMFEI was used for determination of morphology of synthesized complex. Sample was sonicated for a period of 15 min in acetone and was sintered for 2 h before mounting for SEM. The antibacterial activity was studied by paper disk method and data was recorded after 48 h of incubation.

**Ligand-metal ratio:** To confirm the ligand-metal ratio, conductometric titrations using monovariation method were carried out at  $25^\circ\text{C}$ . 0.01 M solution of lansoprazole drug was prepared in 20:80 mixture of DMF and water. Similarly, solutions of neodymium(III) nitrate hexahydrate were prepared in same solvent of 0.02 M concentration. 20 mL of ligand was diluted to 200 mL and titrated against neodymium nitrate solution using monovariation method. Conductance was recorded after each addition. Graph is plotted between corrected conductance and volume of neodymium nitrate added. From the equivalence point in the graph it has been concluded that the complex formation has taken place in the ratio of 1:1:1 (M:L:L). Stability constants and free energy changes were also calculated.

**Preparation of neodymium ternary complex:** For the synthesis of ternary complex, neodymium(III) nitrate hexahydrate was used as an precursor metal salt, which is allowed to react with lansoprazole and uracil. The solid complex was synthesized by mixing the aqueous solution of neodymium nitrate (11.4 g) with ethanolic solution of lansoprazole (3.69 g), uracil (1.1 g) in molar ratio 1:1. The resulting mixtures were than refluxed for 4-5 h at the temperature of  $80^\circ\text{C}$  to give the precipitate. After cooling at room temperature the solid complexes were filtered as fine precipitates. These precipitate was washed twice with water. Then they were dried and stored in a desiccators containing dry calcium chloride.

## RESULTS AND DISCUSSION

The reaction of neodymium(III) nitrate hexahydrate with lansoprazole and uracil afforded in good yield (93 %) of stable purple coloured solid compound with melting point  $237^\circ\text{C}$ . The characterization of molecular structure was made by elemental analyzer's, conductivity and spectroscopy studied.

The value of ligation free energy ( $-\Delta G$ ), enthalpy ( $-\Delta H$ ) and entropy change ( $-\Delta S$ ) of synthesized neodymium ternary complex at 26 and  $36^\circ\text{C}$  in  $\mu = 0.1\text{ M}$  ( $\text{KNO}_3$ ) was reported to be 1.250 Kcal/mol and 1.284 Kcal/mol, 386.34 Kcal/mol and 384.09 Kcal/mol, 38.50 Kcal/mol and 38.28 Kcal/mol, respectively. The compound is freely soluble in DMF, DMSO, ethanol, 1,4-dioxane, nitric acid, insoluble in cold water, acetone, isopropanol and partially in hot water. The molar conductance of synthesized complex is  $81.2\ \Lambda/\text{S cm}^2\text{ mol}^{-1}$ .

**IR spectra:** The characteristics frequencies of the ligands and synthesized neodymium ternary complex are given in Table-1 (Fig. 1). The relevant vibration bands of the free ligand and their mixed ligand complexes are in the region 4000-400  $\text{cm}^{-1}$  [28-30].

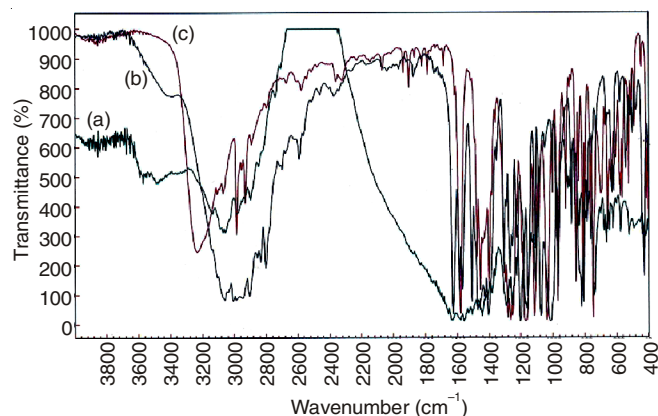


Fig. 1. FTIR spectrum of synthesized neodymium ternary complex (a) synthesized NTC, (b) uracil, (c) lansoprazole

In case of lansoprazole molecule the N-H (aromatic sec. amine) stretching occurs at  $3447\text{ cm}^{-1}$ , whereas sulfoxide ( $\text{S}=\text{O}$ ) stretching occurs at  $1090\text{ cm}^{-1}$ . The aromatic tertiary amine ( $\text{C}=\text{N}$ ) occurs at  $1590\text{ cm}^{-1}$  in lansoprazole. In free uracil molecule the N-H and CO frequency is located in  $1800\text{--}1300\text{ cm}^{-1}$  region. The bending vibration of N(1)-H is at  $1567\text{ cm}^{-1}$  whereas N(3)-H vibration is at  $1408\text{ cm}^{-1}$ . The position and intensity of the bands assignable to the 2-keto group is at  $1750\text{ cm}^{-1}$  [31]. In case of the synthesized ternary complex of neodymium, frequency at about  $3050\text{ cm}^{-1}$  of (N-H) showing that there is no involvement (N-H) group in complex formation, whereas sulfoxide stretching shifts to lower frequencies at about  $45\text{ cm}^{-1}$  due to coordination of the sulfonyl oxygen with neodymium in the synthesized complex. The frequency of ( $\text{C}=\text{N}$ ) bands appears at different region lowered by about  $40\text{ cm}^{-1}$  indicating the coordination of nitrogen atom of ( $\text{C}=\text{N}$ ) with metal. Thus, lansoprazole molecule chelates with neodymium metal ion using its ( $\text{C}=\text{N}$ ) group and ( $\text{S}=\text{O}$ ) group, acting as bidentate ligand. The position and intensity of the bands assignable to the 2 keto group of uracil in the complexes change

TABLE-1  
NORMAL VIBRATION FREQUENCIES ( $\text{cm}^{-1}$ ) OF SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Ligands and synthesized neodymium complex	$\nu(\text{S}=\text{O})$	$\nu(\text{C}=\text{N})$		$\nu(\text{N}(3)\text{--H})$	$\nu(\text{C}(2)=\text{O})$	$\nu(\text{Nd--O})$	$\nu(\text{Coordinated H}_2\text{O})$	
		Stretching	Bending				Stretching	Bending
Lansoprazole	1090	1590	547	—	—	—	—	—
Uracil	—	—	—	1408	1750	—	—	—
$[\text{Nd}(\text{Lanso})(\text{Ura})\cdot 4\text{H}_2\text{O}]\text{NO}_4\cdot n\text{H}_2\text{O}$	1052(w)	1580(w)	520	Dis	1631(w)	755	3450	859

appreciably with respect to free uracil molecule. The bending frequency of the uracil due to N(1)-H remains almost unchanged both in intensity and position while the vibration bands due to N(3)-H at  $1408\text{ cm}^{-1}$  disappears completely in all the complexes. Thus in the synthesized neodymium ternary complex, uracil acts as a chelating ligand binding through its C (2) =O and N (3). In the complex the new band appears at about  $755\text{ cm}^{-1}$ . The appearance of strong band at about  $859\text{ cm}^{-1}$  and about  $3450\text{ cm}^{-1}$  in the spectra of the synthesized neodymium ternary complex indicates the presence of coordinated water.

**$^1\text{H}$  NMR spectra:** To confirm the coordination of the ligands with the neodymium metal ion in the synthesized complexes,  $^1\text{H}$  NMR spectra was recorded and shown in Fig. 2. The important chemical shifts for the ligands and the complexes are given in the Table-2. The  $^1\text{H}$  NMR spectra of the ligand has the expected characteristic signals [32]. The  $\text{CH}_3$  proton shows singlet at  $\delta$  2.16 and O- $\text{CH}_3$  proton at  $\delta$  3.69 ppm the peak observed at  $\delta$  4.71 is attributed to  $\text{CH}_2$  protons. In addition multiplet peak at  $\delta$  6.8-8.2 may be due to aromatic protons and peak at  $\delta$  13.2 is observed due to NH proton of benzimidazole ring. In case of synthesized neodymium ternary complexes, the chemical shifts occurs at low field *i.e.* deshielding of proton occurs in methylene group proving the involvement of electron of S=O in bonding. Signals observed in the complex at region of  $\delta$  8.18-8 due to the azomethine proton are either remained unaffected or shifted slightly to higher field with reference to those of the parent ligand and the position of signal due to NH proton remain unaffected in the synthesized complex. Rest of the chemical shift is more or less same in the ligands and complex. Pure uracil shows the chemical shifts at  $\delta$  10.7 ppm in N-H but in the synthesized complex this have been disappeared showing that there is deprotonation of hydrogen in uracil molecule and the new bond of Nd-N has been made in complex. Thus  $^1\text{H}$  NMR studies confirm the structure of synthesized neodymium ternary complex. The integrated proton ratio also corresponds to the proposed structure.

**Electronic spectra:** Typical electronic spectral data of the neodymium nitrate, ligands and the synthesized complex have been investigated in alcohol. UV-visible spectrum is shown in Fig. 3 and values are reported in Tables 3 and 4. The electronic spectra of the lansoprazole displays absorption bands at 224, 285 which is assigned to  $n\text{-}\pi^*$  and  $\pi\text{-}\pi^*$  transition respectively. The electronic spectra of the uracil displays absorption bands at 224, 269 which are assigned to  $n\text{-}\pi^*$  and  $\pi\text{-}\pi^*$  transition respectively. The electronic spectra of the synthesized complex show a shift towards lower frequency

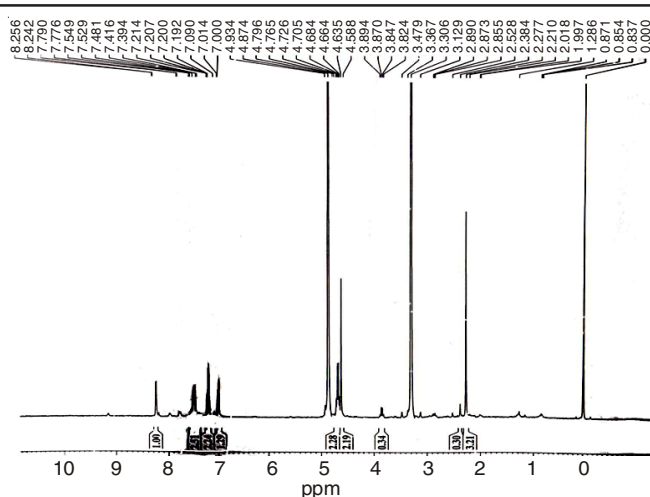


Fig. 2.  $^1\text{H}$  NMR spectrum of synthesized neodymium ternary complex

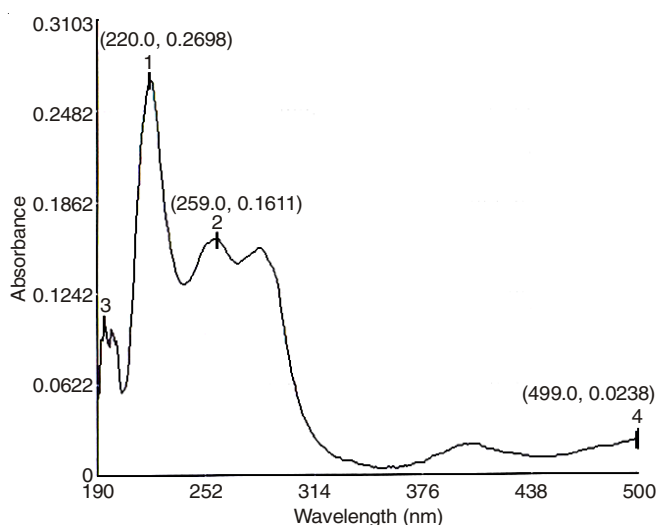


Fig. 3. UV-visible spectrum of synthesized neodymium ternary complex

than that of the ligands. This slight shift was attributed to the effects of the crystal field upon the interelectronic repulsion between the  $4f$  electrons.

Some red shift or nephelauxetic effect is observed in the alcohol solutions of present complex. This red shift is usually accepted as an evidence of a higher degree of covalency than the presence of aqua compounds [33,34]. In the synthesized neodymium complex, marked enhancement in the intensity of the bond has been observed. This red shift of the hyper sensitive bands has been utilized to calculate the nephelauxetic effect ( $\beta$ ) in these chelate complexes. From the  $\beta$  values the covalence factors ( $b^{1/2}$ ), Sinha parameter ( $\delta\%$ ) (metal-ligand covalency percentage) and the covalency angular overlap

TABLE-2  
 $^1\text{H}$  NMR SIGNALS OF SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Kind of proton	Atom No.	Lansoprazole	$[\text{Nd}(\text{Lanso})(\text{Ura})\cdot 4\text{H}_2\text{O}]\text{NO}_3\cdot n\text{H}_2\text{O}$
Aromatic benzimidazole	6,7,8,9	7.35-7.63	7.1-7.7
Aromatic pyridine	15	8.18	8.25
Aromatic pyridine	16	6.98	6.99
Methylene ( $-\text{CH}_2-$ )	12	4.81	4.8(s)
Methyl ( $-\text{CH}_3$ )	24	2.2	2.27
Uracil	—	—	—
N(1)-H	1	10.7	—

TABLE-3  
ELECTRONIC SPECTRAL DATA OF SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Complex	$\lambda_{\max}$ (nm)	Absorbance	Wavenumber ( $\text{cm}^{-1}$ )	$\epsilon_{\max}$ ( $\text{L mol}^{-1}\text{cm}^{-1}$ )	Assignment
[Nd(Lanso)(Ura)-4H <sub>2</sub> O]NO <sub>3</sub> ·nH <sub>2</sub> O	220	0.2698	45454	2698	$n \rightarrow \pi^*$
	259	0.1611	38610	1611	$\pi \rightarrow \pi^*$

TABLE-4  
BONDING PARAMETERS OF SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Complex	Complex band ( $\text{cm}^{-1}$ )	$\beta$	$1-\beta$	$b^{1/2}$	$\delta$ (%)	$\eta$
[Nd(Lanso)(Ura)-4H <sub>2</sub> O]NO <sub>3</sub> ·nH <sub>2</sub> O	45454	0.96364	0.03636	0.09534	3.7731	0.01801
	38610	0.90733	0.09267	0.15220	10.2134	0.04521

parameter ( $\eta$ ) have been calculated using the expressions [33,34] below:

$$b^{1/2} = \frac{1}{2}[(1 - \beta)^{1/2}]$$

$$\delta (\%) = [(1 - \beta)/\beta] \times 100$$

$$\eta = [(1 - \beta)^{1/2}/\beta^{1/2}]$$

The positive values for  $(1-\beta)$  and  $\delta$  % in these coordination compounds suggest that the bonding between metal and ligand is covalent compared with the bonding between the metal and an aqua ion. The values of parameter of bonding ( $b^{1/2}$ ) and angular overlap parameter ( $\eta$ ) were found to be positive, indicating covalent bonding.

**XRD studies:** The X-ray diffraction spectra of the synthesized neodymium ternary complex is shown in Fig. 4. In general XRD pattern are composed of sharp peaks, indicating that synthesized complex has good crystalline structure [35].

**Mass and elemental analysis:** The mass spectrum of the synthesized neodymium ternary complex has been done. The molecular weight and elemental analysis of the complex has been reported in Table-5 (Fig. 5). The mass spectra of the complex shows the molecular ion peaks, supporting the structure of complex [36,37].

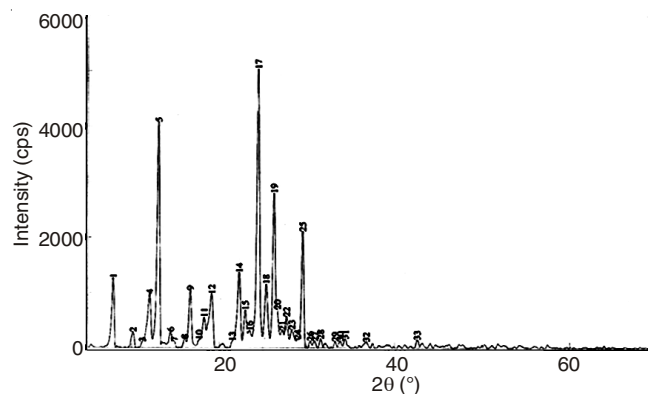


Fig. 4. XRD spectrum of synthesized neodymium ternary complex

**SEM:** The morphological features of the synthesized neodymium ternary complex was obtained by means of scanning electron microscopy (SEM) and is shown in Fig. 6. Several particles were investigated to determine particle size. It has been observed that the particles are well dispersed and almost spherical in shape with particle size in the range of about 25-40  $\mu\text{m}$ .

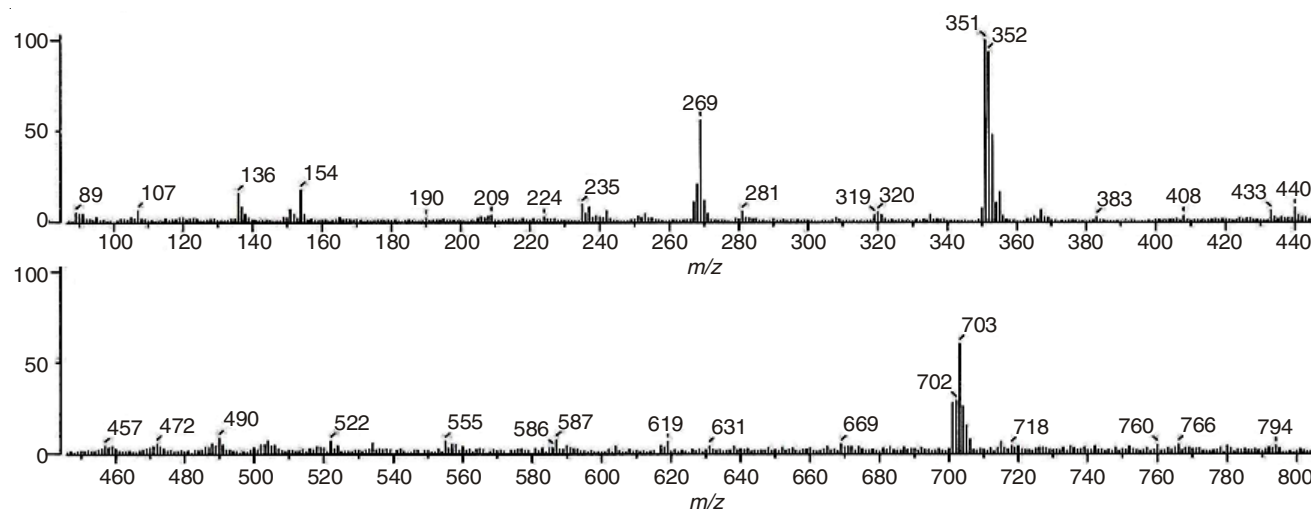


Fig. 5. Mass spectrum of synthesized neodymium ternary complex

TABLE-5  
MASS AND ELEMENTAL ANALYSIS OF SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Complex	Structure	Cal. mass	Spec. mass	Found mass (calculated mass, %)						
				C	H	N	O	F	S	Nd
Nd-L-U	1:1:1:4H <sub>2</sub> O	697	702	34.18 (3.43)	3.7 (3.73)	7.97 (8.03)	15.95 (16.0)	8.11 (8.1)	4.55 (4.5)	25.54 (24.9)



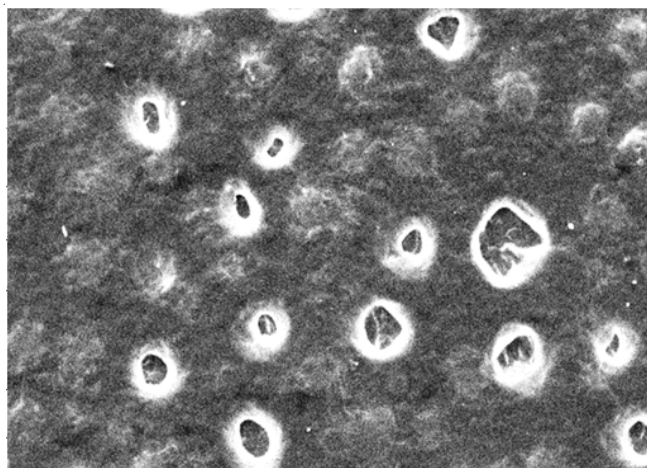


Fig. 6. SEM images of synthesized neodymium ternary complex

**Application in pharmacology:** The antibacterial activity of the ligand, neodymium nitrate and the synthesized neodymium ternary complex were assayed simultaneously against *Streptococcus faecalis* culture by paper disk method at room temperature. The pure metal salt and lansoprazole drug showed activity in *Streptococcus faecalis*. The zones of inhibition against microorganism were measured (in cm) after 48 h of incubation as shown in Table-6. In *Streptococcus faecalis* synthesized complex of neodymium shows higher antibacterial activity as compared to parent drug lansoprazole. The result indicates that the synthesized neodymium complex is more active than free ligand. Increased activity of the complex can be explained on the basis of chelation theory. If the orbital of each metal ion overlaps the ligand orbital increases which enhances the lipophilicity of complexes due to delocalization of electron in the chelate.

TABLE-6  
SENSITIVITY TEST OF LANSOPRAZOLE AND  
SYNTHESIZED NEODYMIUM TERNARY COMPLEX

Metal ion	Inhibition diameter (cm)		
	Lanso	uracil	[Nd(Lanso)(Ura)·4H <sub>2</sub> O]NO <sub>3</sub> ·nH <sub>2</sub> O
Nd	0.9	0.7	1

The proposed scheme and structure of synthesized neodymium ternary complex is reported in Fig. 7.

### Conclusion

The studied ternary complex of neodymium metal showed 1:1:1 (M:LANSO:URA) composition as it is indicated from elemental analyser and exhibit corresponding conductivities suggesting 1:1 electrolytic behaviour. The FTIR data reveals that both the ligand function as bidentate ligands. Lansoprazole molecules chelates with the metal ions using its C=N group and S=O group, the uracil acts as a chelating ligand binding through its C (2) =O and N (3) group.

The <sup>1</sup>H NMR spectra of non-equivalent proton of lansoprazole in complex exhibit chemical shift towards lower field due to complexation with neodymium metal. The electronic spectra data indicates the stereochemistry of synthesized neodymium ternary complex. The morphology of particle was studied by scanning electronic microscopy. The

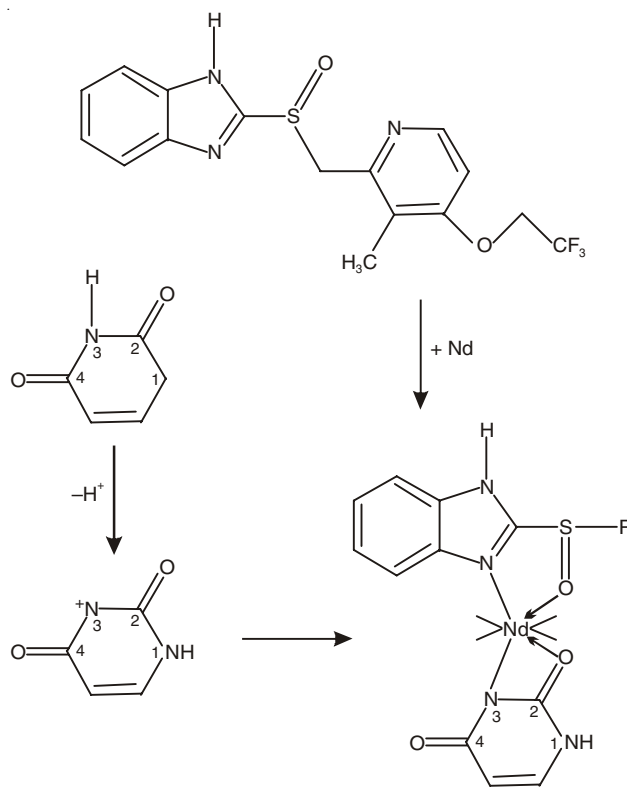


Fig. 7. Proposed scheme and structure of synthesized neodymium ternary complex

results of the study thus indicate the possibility of formation of metal-bridged drug receptor complex during antiulcer activity of the drug. The complex may be formulated as (L<sub>lanso</sub>·Nd·L<sub>Ura</sub>·4H<sub>2</sub>O)X·nH<sub>2</sub>O where X is NO<sub>4</sub><sup>2-</sup>.

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