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SPECTRAL CHARACTERIZATION AND DNA BINDING PROPERTIES OF LANTHANIDE (III) COMPLEXES WITH 2-ACETYLPYRIDINE NICOTINOYLHYDRAZONE (APNH)

B. Moksharagni and K. Hussain Reddy*

Department of Chemistry, Sri Krishnadevaraya University, Anantapuramu-515 003(AP) India

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***Corresponding Author**
Prof. K. Hussain Reddy
Department of Chemistry,
Sri Krishnadevaraya
University, Anantapuramu-
515 003(AP) India.

ABSTRACT.

The lanthanide(III) complexes of general formula of $[Ln(APNH)_2(NO_3](NO_3)_2.nH_2O$ (where, Ln = La, Ce, Pr, Nd, Sm; APNH = 2-acetylpyridine nicotinoyl hydrazone, n = 0, 2 and 5 for La/Ce/Pr, Sm and Nd complexes, respectively) were synthesized under mild reaction conditions with excellent yields. The complexes were characterized based on elemental analysis, molar conductivity, and infrared spectroscopy. Molar conductivity data suggest that the complexes are 1:2 electrolytes. IR spectral data suggest that APNH acts as neutral tridentate ligand. Spectral data of complexes suggest that the ligand binds metal ion through pyridinenitrogen, azomethine-nitrogen and amido-oxygen donor atoms. Electrochemical behaviour of metal complexes was investigated by using cyclic voltammetry. The complexes undergo quasi-reversible one electron reduction. The binding interaction of complexes with CT-DNA was investigated using absorption spectrophotometry. Based on spectral changes, *groove binding* of complexes to DNA is suggested.

KEYWORDS: Lanthanide(III) complexes, 2-Acetylpyridine nicotinoylhydrazone, Spectral characterization, DNA binding.

INTRODUCTION

Investigations of lanthanide complexes with polydentate ligands have received considerable attention because of their potential applications in various fields.[1-11]. Hence, the synthesis of and characterization of newer lanthanide complexes is a potential field of research in inorganic chemistry. Though Sacconi has reported.[12] lanthanide complexes of acetylacetone nicotinoyl hydrazone in the year 1954, a literature review.[13-15] indicated that the study of such complexes is relatively less when compared with transition metal complexes with this class of ligands.The chemistry of lanthanide complexes is of interest owing to their applications in biology and medicine.[16, 17]. Heterocyclic hydrazones as well as their metal complexes gained importance because of their pharmacological properties.[18-20]. Metal complexes of isonicotinoylhydrazones exhibit antitumour.[21] and antibacterial activity.[22] There is also much interest in the development of artificial nucleases. Artificial metallonucleases require ligands which effectively deliver metal ions to the vicinity of DNA. Investigation of metal-DNA interactions.[23] has been an area of active research.[24, 25]. Studies on chemical modification of nucleic acids with lanthanide complexes are of great interest in the design of chemotherapeutic drugs, regulation of gene expression and design of tools for molecular biology.[26]. In the light of the above and in continuation of earlier work.[28, 29] on DNA binding activities of lanthanide(III) metal complex, herein we report synthesis, spectral characterization and DNA binding properties of lanthanide(III) complexes of 2-acetylpyridine nicotinoylhydrazone for the first time.

EXPERIMENTAL

Lanthanide nitrates, 2-acetylpyridine and nicotinic acid hydrazide , purchased from Aldrich chemicals wereused without further purification. Lanthanide salts were stored in desiccators to prevent hydration. CT DNA was purchased from Genie Biolabs, Bangalore, India.

Synthesis of 2-acetylpyridine nicotinoylhydrazone (APNH)

A 5 mmol of 2-acetyllpyridine (0.56 mL) dissolved in 20 mL of methanol was added to an methanolic solution of nicotinic acid hydrazide (0.685 g, 5 mmol). The contents were taken in a round bottom flask stirred for 20 min. An yellow colored product was formed. It was collected by filtration, washed with a few drops of ethanol and dried in vacuum. Yield of the product was 85%, m.p.: 162-164 oC. Physicochemical and analytical data of APINH are given in Table 1

General procedure for the synthesis of lanthanide complexes

To the ligand (0.480 g, 2 mmol) dissolved in 20 mL of methanol, lanthanum(III) nitrate hexahydrate [$Ln(NO_3)_3.6H_2O$] (1 mmol) dissolved in 10 mL of methanol was added. The for 2-4 h. Upon cooling solid substance was formed. It was collected by filtration, washed with 10 mL of hexane and dried in vacuum. Physicochemical and analytical data of lanthanide complexes are included in Table 1.

Physical measurements

The elemental analyses were performed using a Perkin-Elmer 2400 CHNS elemental analyzer. The molar conductance of the complexes in DMF (10^{-3} M) solution was measured at 28^0C with a Systronic model 303 direct-reading conductivity bridge. The magnetic measurements were recorded at room temperature at various field strengths using Lakeshore VSM 7410 magnetometer. The electronic spectra were recorded in DMF with a Perkin Elmer UV Lamda – 50 spectrophotometer. FT-IR spectra in KBr disc were recorded in the range 4000-400 cm-1 with a Perkin Elmer spectrum 100 spectrometer. The cyclic voltammetry was performed with a CH instruments 660C Electrochemical analyzer and a conventional three electrode, Ag/AgCl reference electrode, glassy carbon working electrode and platinum counter electrode. Nitrogen gas was purged and measurements were made on the degassed (N_2 bubbling for 5 min) complex solution in DMF (10^{-3} M) containing 0.1 M tetrabutylammonium hexaflourophosphate (TBAHP) as the supporting electrolyte

a. Electronic spectra

The electronic spectrum of ligand and their corresponding lanthanide(III) complexes are recorded in DMF. Typical electronic spectra (a) APNH ligand (b) $[La(APNH)_2(NO_3)](NO_3)_2$ complex are given in **Figure 9.2.** In the electronic spectra of complexes a broad peak is observed in the high energy region at 33560 cm^{-1} assigned to π - π^* transition. A strong peak is observed in the low energy region (27030 – 27330 cm^{-1}) of electronic spectra of complexes. It is assigned to charge transfer transition. Electronic spectral data are given in **Table 9.2.** Thus the weak f-f transitions occurring in the region due to lanthanide ion in the complexes are obscured by the intense ligand bands. Also the ligand band remains largely unaffected on complexation and insensitive to the lanthanide ion. No absorption band due to f-f transition of lanthanide(III) ions could be located in the visible region in the spectra of complexes. This is probably due to the fact that the f-f bands are weak and obscured by the intense charge transfer bands.[30]

Infrared spectra

The IR spectrum of APNH ligand is devoid of absorptions characteristic of an NH_2 function. A strong band at 1662 cm^{-1} is assigned to $\nu_{C=O}$ vibration. The band due to $\nu_{C=N}$ vibration is observed at 1581 cm^{-1} as strong band. The $\nu_{N\text{-}H}$ vibration occurs at 3211 cm^{-1}. FT-IR spectrum of $[La(APNH)_2(NO_3)](NO_3)_2$ complex is shown in **Figure 9.3**.

The appearance of νNH band in IR spectra of complexes suggests that the ligand remains in keto form in coordination. A considerable lowering of the ν$_{(C=O)}$ frequency is observed in the spectra of complexes, indicating decrease in the stretching force constant of the C=O bond as consequence of the coordination of the oxygen atom to the metal ion This band appears in spectra of complexes in stretching vibration in the free ligand form is not affected precluding the involvement of >NH group in 1631-1633 cm^{-1} region. IR data suggest that the hydrazone ligands act as neutral tridentate ligand.

The IR spectrum of the complexes demonstrates the presence of coordinated nitrate. The two strong bands are observed in complexes due to the presence of coordinated nitrates. The two strong bands associated with asymmetric and symmetric stretch of coordinated to NO_3^- (C_{2v}) group appear in the range 1434- 1468 (ν_1) and 1214-1293 (ν_4) cm^{-1}. The frequency separation Δν (ν_1- ν_4) increases as the coordination of nitrate group increases from monodentate to bidentate and/ or bridging. The magnitude of Δν is used to establish the type of nitrate coordination. In the present complexes the Δν is in between 165-224 cm^{-1} and is typical of bidentate bonding of nitrate.[31] The vibrational band is observed around 1380 cm^{-1} in IR spectra of complexes indicating the presence of ionic nitrate. (D_{3h} symmetry, free NO_3^- ion) The data indicate that the complexes contain free ionic nitrate and coordinated bidentate nitrate groups. The new bands in 412-418 and 530 - 543 cm^{-1} regions are assigned to ν(Ln–O) and ν(Ln–N) vibration respectively.

Based on molar conductivity, magnetic moments, electronic spectral data, a tentative and general structure for the complexes is given in **Fig 9.4.**

b. Electrochemical studies

Redox behavior of the lanthanide(III) complexes has been investigated by cyclic voltammetry in DMF using 0.1M tetrabutylammonium hexaflourophosphate (TBAHP) as supporting electrolyte. The cyclic voltammetric profile of APNH ligand and $[Nd(APNH)_2(NO_3)](NO_3)_2$ complex are shown in **Figures 9.5** and **9.6** respectively.

As the scan rate increases separation between cathodic and anodic peaks increases suggesting quasi-reversible character of cyclic voltammogram. The electrochemical data of the complexes are presented in **Table 9.6.**

Repeated scans at various scan rates suggest the presence of stable redox species in solution. From the $E_{1/2}$ values, it may be inferred that Ln(III) complexes undergo reduction to their respective Ln(II) complexes.[32,33] The complexes have large separation (160-289 mv) between anodic and cathodic peaks indicating quasi-reversible character, the log K_c and $_{\Delta}G^0$ values suggest that the complexes are stable in solution state.

c. DNA binding studies

Electronic absorption spectroscopy is an effective method for examining the interaction of DNA with metal complexes. The binding interaction of complexes with CT-DNA was monitored by comparing their absorption spectra with and without CT-DNA. All the complexes exhibit an intense absorption band due to $\pi \rightarrow \pi^*$ transition. Absorption spectra of $[Nd(APNH)_2(NO_3)](NO_3)_2$ in the absence and in presence of CT-DNA are shown **Figure 9.7**.

The intrinsic binding constants (K_b), were determined by using the equation,

$$[DNA] / (\varepsilon_a - \varepsilon_f) \quad = \quad [DNA] / (\varepsilon_b - \varepsilon_f) + 1/ K_b (\varepsilon_b - \varepsilon_f) \qquad \text{----------------} \ (1)$$

Where [DNA] is the concentration of DNA in base pairs, ε_a, ε_b and ε_f are apparent extinction coefficient ($A_{obs/}$ [M]), the extinction coefficient for the metal (M) complex in the fully bound form and the extinction coefficient for free metal (M) respectively. A plot of [DNA] / (ε_a-ε_f) versus [DNA] gave a slope of 1/ (ε_b-ε_f), and vertical intercept equal to 1/ K_b (ε_b–ε_f); Kb was calculated from these values. The binding constants **(Table 9.8)** suggest that the complexes bind DNA very strongly. The binding constants **(Table 9.8)** for suggest that the complexes bind DNA very strongly. On addition of DNA, the absorbance of the complexes decreases (hypochromism) and absorption maximum of all complexes is shifted (1-3 nm) to higher wavelength (bathochromism). The sharp isobestic point (307 nm) in the absorption curves **(Figure 9.7)** suggests that there is only one mode of binding.[34, 35]

Small bathochromic shift (1 nm), low binding constant (K_b) 10^4 values and bulky nature of complex suggest groove binding of complexes to DNA.

Table 9.1: Analytical and physico-chemical properties of APNH ligand and its lanthanide(III) complexes

Complex	Colour (Yield, %)	F. Weight	M.P* (°C)	Analysis Found (calc. %)			Λ_M †
				C	H	N	
$[La(APNH)_2(NO_3)](NO_3$	White	804	210-212	38.76	2.98	18.13	109

$)_2$	(71)			(37.70)	(3.10)	(19.10)	
$[Ce(APNH)_2(NO_3)](NO_3)_2$	Yellow (62)	806	180-182	38.70 (37.50)	2.97 (3.12)	19.10 (18.20)	120
$[Nd(APNH)_2(NO_3)](NO_3)_2$	Gray (56)	810	182-184	38.50 (37.55)	2.96 (3.11)	18.00 (19.10)	90
$[Pr(APNH)_2(NO_3)](NO_3)_2$	Green (69)	806	192-194	37.66 (38.60)	2.97 (3.10)	19.08 (18.11)	98
$[Sm(APNH)_2(NO_3)](NO_3)_2$	Yellow (80)	816	178-180	38.22 (37.30)	2.94 (2.80)	17.86 (18.80)	86

* Decomposes.

† Units: Ω^{-1} cm^2 mol^{-1} in DMF.

Table 9.2: Electronic Spectral data (cm^{-1}) of lanthanide(III) complexes in solution state*

Complex	λ_{max} (nm)	ε†	Band assignment
APNH (ligand)	297(33670)	560	π - π*
$[La(APNH)_2(NO_3)](NO_3)_2$	298(33560) 366(27330)	620 870	π - π* CT
$[Ce(APNH)_2(NO_3)](NO_3)_2$	298(33560) 366(27330)	1330 1030	π – π* CT
$[Nd(APNH)_2(NO_3)](NO_3)_2$	298(33560) 367(27250)	270 400	π – π* CT
$[Pr(APNH)_2(NO_3)](NO_3)_2$	298 (33560) 366(27330)	880 1370	π – π* CT
$[Sm(APNH)_2(NO_3)](NO_3)_2$	298(33560) 370(27030)	270 420	π – π* CT

* Spectra of the complexes were recorded in DMF solvent.

† Molar absorptivity Units, L. mol^{-1} cm^{-1}.

Table 9.3: Infrared Spectral data (cm^{-1}) for the APNH ligand and its lanthanide(III) complexes

Complex	ν(N-H)	ν(C=O)	ν(C=N)	$\nu(NO_3)$				
				ν_1	ν_2	ν_3	ν_4	ν_1-ν_4
APNH (ligand)	3211	1662	1581	…	…	…	…	…
$[La(APNH)_2(NO_3)](NO_3)_2$	3066	1647	1595	1427	1033	781	1255	172
$[Ce(APNH)_2(NO_3)](NO_3)_2$	3054	1612	1551	1474	1159	778	1351	123
$[Nd(APNH)_2(NO_3)](NO_3)_2$	3068	1624	1598	1450	1016	827	1251	199
$[Pr(APNH)_2(NO_3)](NO_3)_2$	3047	1613	1553	1414	1161	822	1250	164
$[Sm(APNH)_2(NO_3)](NO_3)_2$	3052	1614	1590	1470	1075	813	1278	192

Table 9.5: Cyclicvoltametric data of lanthanide(III) complexes

Complex	Redox couple	E_{pc} V	E_{pa} V	ΔE (mv)	$E_{1/2}$	log K_c^a	$-\Delta G^{o}$ b
APNH (ligand)	…	-0.884	…	…	…	…	…
$[La(APNH)_2(NO_3)](NO_3)_2$	III/II	-1.442	-1.250	192	1.346	0.178	1004

$[Ce(APNH)_2(NO_3)](NO_3)_2$	III/II	-1.384	-1.220	164	1.302	0.204	1176
$[Nd(APNH)_2(NO_3)](NO_3)_2$	III/II	-1.590	-1.430	160	1.510	0.326	1872
$[Pr(APNH)_2(NO_3)](NO_3)_2$	III/II	-0.995	-0.825	170	0.912	0.197	1134
$[Sm(APNH)_2(NO_3)](NO_3)_2$	III/II	-0.909	-0.620	289	0.764	0.116	667

^{a} $\log K_c = 0.434ZF/RT\Delta E_p$; ^{b} $\Delta G^0 = -2.303RT\log K_c$

Table 9.6: Electronic absorption data upon addition of CT-DNA to the complex

Complex	**λ_{max} (nm)**		**Δλ/nm**	**H (%)**	**K_b (M^{-1})**
	free	**bound**			
$[La(APNH)_2(NO_3)](NO_3)_2$	291	293	2	+20.05	1.68×10^4
$[Ce(APNH)_2(NO_3)](NO_3)_2$	290	291	1	+1.39	4.23×10^4
$[Nd(APNH)_2(NO_3)](NO_3)_2$	345	344	1	+17.61	9.84×10^4
$[Pr(APNH)_2(NO_3)](NO_3)_2$	340	341	1	+20.56	1.15×10^4
$[Sm(APNH)_2(NO_3)](NO_3)_2$	343	346	3	+15.75	1.57×10^4

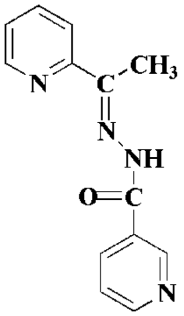

Fig 9.1: The Structure of APNH ligand

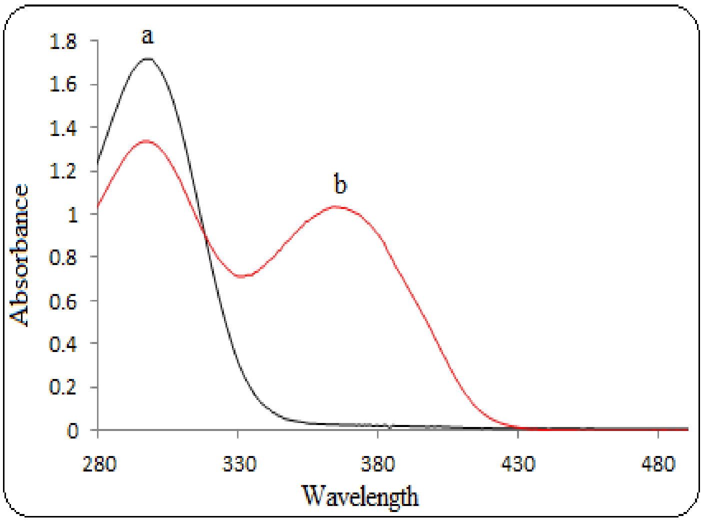

Figure 9.2: Electronic spectrum of APNH ligand and $[Ce(APNH)_2(NO_3)](NO_3)_2$ complex

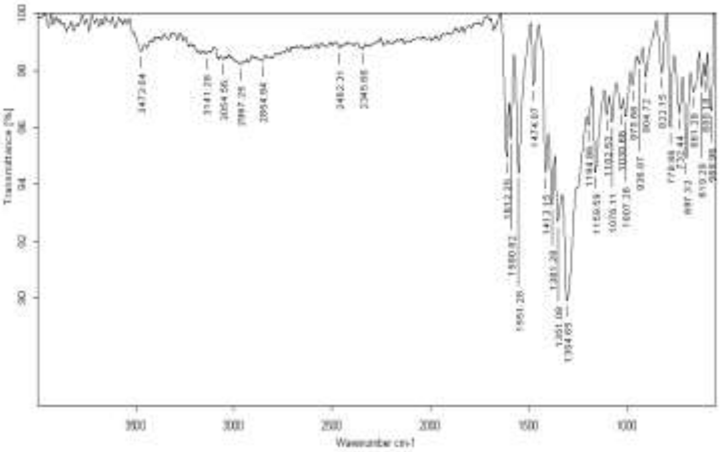

Fig 9.3: FT-IR spectrum of $[Ce(APNH)_2(NO_3)](NO_3)_2$ complex.

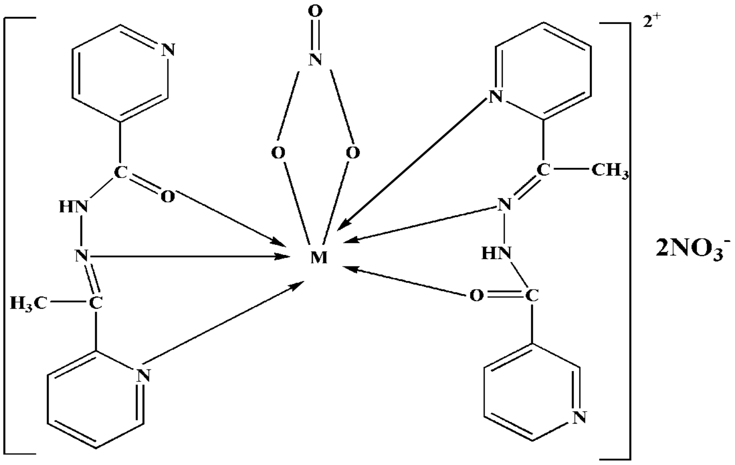

Fig 9.4: General structure for lanthanide(III) complexes. M = La, Ce, Pr, Nd and Sm.

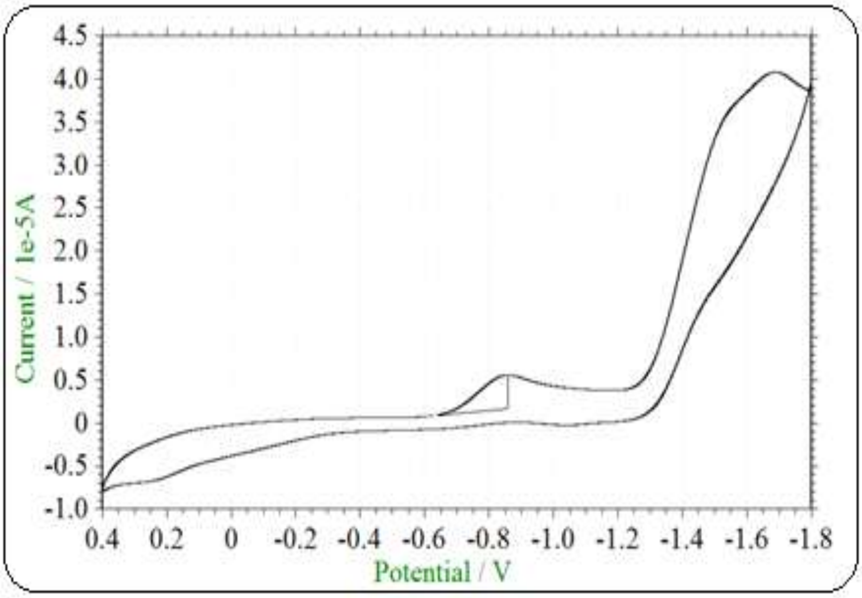

Fig 9.5: Cyclic voltammetric profile of APNH ligand at scan rate 25 mVs^{-1}.

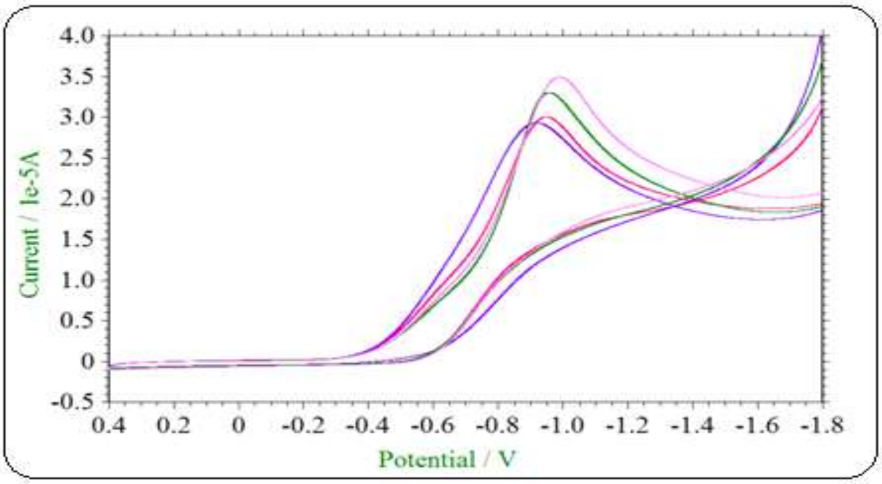

Fig 9.6: Cyclicvoltammogrms of $[Sm(APNH)_2(NO_3)](NO_3)_2$ complex at different scan rates 25, 50, 75, 100 mVs^{-1}.

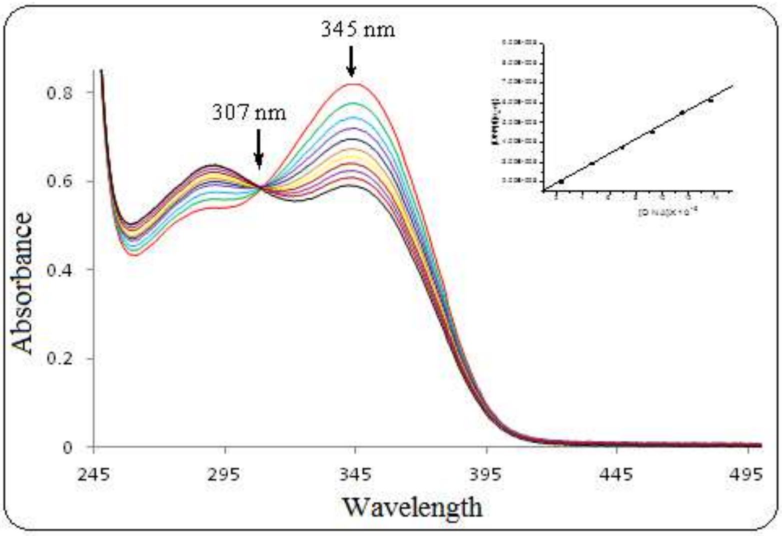

Fig 9.7 : (A) Absorption spectra of $[Nd(APNH)_2(NO_3)](NO_3)_2$ in the absence and in the presence of increasing concentration of CT-DNA ; (B) A plot of [DNA] / ($\varepsilon_a - \varepsilon_f$) versus [DNA]

CONCLUSIONS

Lanthanide complexes of 2- acetylpyridine nicotiniylhydrazone have been synthesized and characterized based on physicochemical spectral data. A general structure is proposed for the complexes. DNA binding properties of complexes are investigated using absorption spectroscopy.

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