



## SYNTHESIS, SPECTRAL CHARACTERIZATION AND DNA BINDING PROPERTIES OF DINUCLEAR NICKEL (II) COMPLEXES WITH PYRIDINE BASED HYDRAZONES

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### ABSTRACT

Dinuclear nickel(II) complexes of functionalized heterocyclic hydrazones, viz. 2-acetylpyridine acetylhydrazone (APAH), 2-acetylpyridine benzoylhydrazone (APBH), 2-benzoylpyridine acetylhydrazone (BPAH), 2-benzoylpyridine benzoyl hydrazone (BPBH) have been synthesized and characterized on the basis of elemental analysis, molar conductivity measurements, magnetic susceptibility, electronic and infrared spectral data. Electrolytic nature of complexes is investigated by conductivity studies. IR spectral data suggest that the ligands act as neutral trifunctional NNO-donor system. Electronic spectral data suggest octahedral geometry for the complexes. Electrochemical behavior of metal complexes indicated quasi-reversible one electron reduction. DNA binding properties of complexes are investigated using UV- visible spectroscopy. Absorption titration studies revealed that these complexes bind to calf-thymus DNA strongly through intercalation involving a strong  $\pi$ -stacking interaction between the aromatic chromophore (pyridine moiety) and base pairs of DNA

**KEY WORDS:** Synthesis, nickel(II) complexes, pyridine hydrazones, spectral studies, DNA binding properties.



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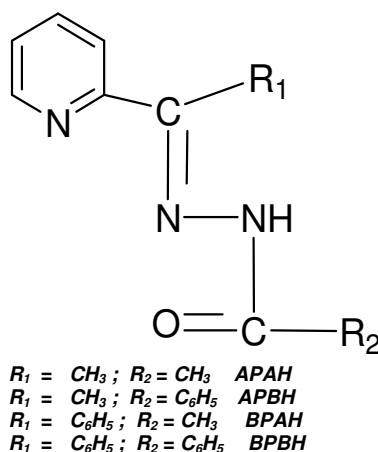
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## INTRODUCTION

Binding studies of small molecules of DNA are very important in the development of DNA molecular probes and new therapeutic reagents<sup>1</sup>. Transition metal complexes have attracted considerable attention as catalytic systems for use in the oxidation of organic compounds<sup>2</sup>, probes in electron transfer reactions involving metalloproteins<sup>3</sup>, and intercalators with DNA<sup>4</sup>. Numerous biological experiments have demonstrated that DNA is the primary intracellular target of anticancer drugs; interaction between small molecules and DNA can cause damage in cancer cells, blocking the division and resulting in cell death<sup>5-7</sup>. Since the heterocyclic unit is the key-building block for a variety of compounds which have crucial roles in the functions of biologically important molecules, there is a constant and growing interest over the past few years for the synthesis and biological studies of pyridine based derivatives<sup>8-10</sup>. Since the characterization of urease as a nickel enzyme in 1975, the knowledge of the role of nickel in bioinorganic chemistry has been rapidly expanding<sup>11</sup>. The interaction of Ni(II) complexes with DNA appears to be mainly dependent on the structure of the ligand exhibiting intercalative behavior<sup>12-14</sup>. Metal complexes of hydrazones have wide

applications in biological processes<sup>15-16</sup> and as catalysts in chemical and petrochemical industries<sup>17</sup>. The bioactivity of heterocyclic hydrazones as well as their metal complexes is of interest, especially due to their pharmacological properties<sup>18</sup>. Metal complexes of aroylhydrazones exhibit antitumour<sup>19</sup> and antibacterial activity<sup>20</sup>. There is also much interest in the development of artificial nucleases. Artificial metallo-nucleases require ligands which effectively deliver metal ions to the vicinity of DNA. An investigation on metal-DNA interactions has been an area of active research<sup>21</sup>. Studies on chemical modification of nucleic acids with transition metal complexes are of great interest in the design of chemotherapeutic drugs, regulation of gene expression and design of tools for molecular biology<sup>22</sup>. Nickel(II) complexes have been shown to bind the DNA bases at the N(7) of purines and N(1) of pyrimidines<sup>23</sup>. In the light of the above and in continuation of our ongoing research work<sup>24, 25</sup>, a series of functionalized hydrazones (Figure 1) and their nickel(II) complexes have been synthesized and characterized. The ligands are synthesized by using corresponding precursors.

**Figure 1 – A**  
**general structure for ligands**



## MATERIALS AND METHODS

Analytical grade 2-acetylpyridine, 2-benzoylpyridine, acetylhydrazide and benzhydrazide

were purchased from Sigma-Aldrich Chemicals Pvt. Ltd. India. Copper chloride was purchased from Merck chemicals. The solvents used in the synthesis of ligand and

metal complexes were distilled before use. Calf-Thymus DNA (CT-DNA) was purchased from Genie 79 Bio labs, Bangalore, India. All other chemicals were of reagent grade quality and used without further purification.

### Preparation of ligands

Hot aqueous solution of hydrazide 0.5 mmol was added to a boiling solution of methanolic solution of carbonyl compound (0.5 mmol). The reaction mixture was heated under reflux for 1 hr. pale yellow coloured crystalline products were formed in cooling the reaction mixture. The hydrazones collected by filtration, washed several times with hot water and dried in vacuo. The ligands were recrystallized from methanol.

**2-Acetylpyridine acetoxyhydrazone (APAH)**, Yield 85%, M.P. 162-164°C, elemental analysis C-61.32(61.00); H- 6.50 (6.25); N- 24.0 (23.71); IR spectra, 3185, 1678, 1620  $\text{cm}^{-1}$  are assigned to  $\nu(\text{NH})$ ,  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}=\text{N})$  stretching vibrations respectively. The  $^1\text{H-NMR}$  spectra ( $\text{CDCl}_3$ , ppm);  $\delta$  2.4 (singlet, 3H),  $\delta$  2.5 (singlet, 3H),  $\delta$  7.25 (singlet, 1H),  $\delta$  7.75-7.85 (multiplet, 4H), are respectively assigned to  $-\text{CH}_3$  (carbonyl),  $-\text{CH}_3$  (hydrazine),  $\text{NH-}$  and pyridine protons. LC-MS spectrum of HL shows molecular ion peaks at ( $m/z$ ) 177.

**2-acetylpyridine benzoylhydrazone (APBH)**, Yield 80%, M.P. 145-147°C, elemental analysis C-68.75(70.27); H- 5.50 (5.47); N-17.12 (17.56); IR spectra, 3177, 1654, 1616  $\text{cm}^{-1}$  are assigned to  $\nu(\text{NH})$ ,  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}=\text{N})$  stretching vibrations respectively. The  $^1\text{H-NMR}$  spectra ( $\text{CDCl}_3$ , ppm); at  $\delta$  2.5 (singlet, 3H),  $\delta$  7.25 (singlet, 1H),  $\delta$  7.75-7.85 (multiplet 9 H), are respectively assigned to  $-\text{CH}_3$ ,  $>\text{NH-}$  and aromatic (pyridine + phenyl ring) protons. LC-MS spectrum of HL shows molecular ion peaks at ( $m/z$ ) 239.

**2-benzoylpyridine acetoxyhydrazone (BPAH)**, Yield 83%, M.P. 145-147°C, elemental analysis C-71.20(70.27); H- 5.70 (5.45); N-17.96 (17.56); IR spectra, 1668, 1586  $\text{cm}^{-1}$  are assigned to  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}=\text{N})$  stretching vibrations respectively. The  $^1\text{H-NMR}$  spectra ( $\text{CDCl}_3$ , ppm);  $\delta$  1.80 (singlet, 3H),  $\delta$  7.40 (singlet, 1H),  $\delta$  7.42- 8.80 (multiplet 9H), are respectively assigned to  $-\text{CH}_3$ ,  $>\text{NH-}$  and aromatic (pyridine + phenyl ring) protons. LC-MS spectrum of HL shows

molecular ion peaks at ( $m/z$ ) 239. **2-benzoylpyridine benzoylhydrazone (BPBH)**, Yield 72%, M.P. 135-137°C, elemental analysis C-75.9(75.72); H- 5.23 (5.01); N-14.02 (13.94); IR spectra, 1666, 1586  $\text{cm}^{-1}$  are assigned to  $\nu(\text{C}=\text{O})$  and  $\nu(\text{C}=\text{N})$  stretching vibrations respectively. The  $^1\text{H-NMR}$  spectra ( $\text{CDCl}_3$ , ppm);  $\delta$  7.22 (singlet 1H),  $\delta$  7.30- 8.80 (multiplet 13 H) are respectively assigned to imine ( $>\text{NH-}$ ) and aromatic (one pyridine + two phenyl ring) protons. LC-MS spectrum of HL shows molecular ion peaks at ( $m/z$ ) 239.

### Preparation of complexes

The complexes were prepared by mixing hot aqueous solution of  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$  and ligand in a molar ratio of 1:1. To the boiling solution of ligand (0.01 mol) in methanol (100 ml) was added  $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$  (0.01 mol) dissolved in a minimum quantity of water and the reaction mixture was heated under reflux for 2h. Crystalline complexes which separated out were collected by filtration, washed with hot water, small quantity of methanol and hexane and dried in *vacuo*. Analytical data of complexes are given in Table 1. The elemental analyses were performed at RSIC, CDR I Lucknow. Molecular weights of the complexes were determined by using Rast's method. Magnetic measurements of complexes were carried out at 298 K in Faraday's magnetic susceptibility balance (Sherwood Scientific, Cambridge, UK). High purity pentahydrated copper sulphate was used as a standard. The conductivity measurements were recorded using ELICO CM model 162 conductivity cell at  $298 \pm 2$  in dry and purified DMF. The electronic spectra of metal complexes were recorded in DMF with UV lamda50 (Perkin Elmer) spectrophotometer. The infrared spectra were recorded in the range 4000-400  $\text{cm}^{-1}$  with Perkin Elmer spectrum 100 spectrometer in KBr discs. The cyclic voltammetry was performed with a CH Instruments 660C electrochemical analyzer and a conventional three electrode configuration with glassy carbon working electrode, silver/silver chloride reference electrode and platinum counter electrode. Nitrogen was used as a purge gas and all solutions were 0.1M concentration in

tetrabutylammonium hexafluorophosphate (TBAPF<sub>6</sub>) supporting electrolyte.

### DNA binding experiments

Interaction of complexes with calf thymus DNA was studied by electronic absorption spectroscopy. All the experiments involving interaction of the complexes with CT-DNA were carried out in a water buffer containing 5mM tris (hydroxyl methyl) ammonia methane (Tris) and 50mM NaCl and adjusted to pH. 7.0 with HCl. The solution of CT-DNA in 5mM Tris-HCl/50mM NaCl gave a ratio of UV absorbance at 260 and 280 nm ( $A_{260}/A_{280}$ ) of 1.8–1.9, indicating that the DNA is sufficiently free from proteins<sup>26</sup>. A concentrated stock solution of DNA was prepared in 5 mM Tris-HCl/50 mM NaCl in water at pH 7.0 and the concentration of CT-DNA was determined per nucleotide by taking the absorption coefficient ( $6,600 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) at 260 nm<sup>27</sup>. Stock solutions are stored at 4°C and were used after no more than 4 days. Doubly distilled water was used to prepare buffer solutions. Absorption titrations were performed by

maintaining the metal complex concentration  $2 \times 10^{-5} \text{ M}$  and varying the nucleic acid concentration ( $0-26.4 \times 10^{-6} \text{ M}$ ). Absorption titration experiments were performed by maintaining the metal complex concentration constant while gradually increasing the concentration of CT-DNA within 0-100  $\mu\text{M}$ .

## RESULTS AND DISCUSSION

The complexes are stable at room temperature, non-hygroscopic, sparingly soluble in water, partially soluble in methanol, ethanol and readily soluble in acetonitrile (CH<sub>3</sub>CN), DMF and DMSO. The analytical data (Table 1) are consistent with the proposed molecular formulae of complexes. The molar conductivity data suggest that the complexes are 1:2 electrolytes. The observed magnetic moment values for complexes are subnormal possibly due to the presence of antiferromagnetically coupled metal centers. Electronic spectral data of metal complexes are summarized in Table 2. In the spectra of

**Table 1**  
**Physico-chemical and analytical data of nickel(II) complexes**

Complex	Colour (yield,%)	Mol. Wt.	Analyses Found (Calc.) (%)				Melting Point* (°C)	$\mu_{\text{eff}}$ (BM)	Molar conductivity ( $\Omega \text{ cm}^2 \text{ mol}^{-1}$ )
			C	H	N	Ni			
[Ni(APAH)Cl] <sub>2</sub> Cl <sub>2</sub>	LightGreen (63)	613 (613.58)	36.72 (35.23)	3.89 (3.61)	14.12 (13.69)	19.50 (19.13)	291-293 <sup>d</sup>	1.26	66.5
[Ni(APBH)Cl] <sub>2</sub> Cl <sub>2</sub>	Green (47)	738 (737.92)	45.87 (45.57)	4.01 (3.55)	12.98 (11.39)	16.21 (15.90)	>300	1.4	71.0
[Ni(BPAH)Cl] <sub>2</sub> Cl <sub>2</sub>	Green (52)	738 (737.72)	46.89 (45.58)	4.12 (3.55)	12.84 (11.39)	16.22 (15.91)	285-287 <sup>d</sup>		80.01
[Ni(BPBH)Cl] <sub>2</sub> Cl <sub>2</sub>	LightGreen (55)	862 (861.87)	53.20 (52.95)	4.95 (3.50)	10.55 (9.75)	14.23 (13.61)	>300		82.04

\*Decomposes

**Table-2**  
**Electronic spectral data( $\text{cm}^{-1}$ ) of metal complexes in solution state\***

Complex	Intraligand transition	Charge transfer Transition	d-d transition		
[Ni(APAH)Cl] <sub>2</sub> Cl <sub>2</sub>	37453	27322	25595	15925	10402
[Ni(APBH)Cl] <sub>2</sub> Cl <sub>2</sub>	32258	27100	25706	15385	10060
[Ni(BPAH)Cl] <sub>2</sub> Cl <sub>2</sub>	37693	26246	25255	15592	10520
[Ni(BPBH)Cl] <sub>2</sub> Cl <sub>2</sub>	37735	-	25752	15097	10095

\* Spectral of complexes were recorded in DMF solvent

metal complexes, a strong band in the range 26246 - 27322  $\text{cm}^{-1}$  may be associated with M-L charge transfer transition. The high energy bands of moderately intense band in the range 32258 - 37735 are assigned to intra-ligand transition band in the spectra of all metal complexes. Nickel(II) complexes exhibit three d-d bands in favour of octahedral geometry<sup>28</sup>. The bands from lower energy to higher energy are attributable to  ${}^3A_{2g} \rightarrow {}^3T_{1g}$ ;

${}^3A_{2g} \rightarrow {}^3T_{2g}$  and  ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$  transitions respectively. The spectral data are utilized to compute important ligand field parameters such as 10 Dq, Racah parameter or interelectronic repulsion constant (B) and *Nephelauxetic ratio*( $\beta$ ) using ligand field theory of spin allowed transitions of  $d^8$  configuration<sup>28</sup>. Electronic spectral data and ligand field parameters of nickel complexes are given in Table 3.

**Table 3**  
**Ligand field parameters of nickel (II) complexes**

Complex	$\nu_1$	$\nu_2$	$\nu_3$	B	$\beta$	%CC	10Dq	$\nu_2-\nu_1$	$\nu_2/\nu_1$	LFSE
[Ni(APAH)Cl] <sub>2</sub> Cl <sub>2</sub>	10402	15925	25595	689	0.0659	34.1	10402	4523	1.43	29.72
[Ni(APBH)Cl] <sub>2</sub> Cl <sub>2</sub>	10060	15385	25706	727	0.698	30.2	10060	5325	1.53	28.74
[Ni(BPAH)Cl] <sub>2</sub> Cl <sub>2</sub>	10520	15592	25255	619	0.594	40.6	10520	4072	1.38	30.06
[Ni(BPBH)Cl] <sub>2</sub> Cl <sub>2</sub>	10095	15097	25752	704	0.676	32.4	10095	5002	1.49	28.84

\*Percentage of covalent character

IR spectra of ligands are compared with those of metal complexes to determine donor atoms of ligand. Important IR spectral bands and their assignment are given in Table 4. The IR spectra of ligands have several prominent peaks due to  $\nu_{N-H}$ ,  $\nu_{C=O}$  and  $\nu_{C=N}$  stretching modes, respectively. In the spectra of

complexes,  $\nu_{N-H}$  and  $\nu_{C=O}$  bands are present suggesting that the hydrazone acts as neutral ligand. The  $\nu_{C=N}$  in the spectrum of free hydrazone is shifted to lower frequency in the spectra of complexes suggesting the involvement of azomethine nitrogen in chelation. IR data (Table-4) suggest that the

**Table 4**  
**Important IR Spectral bands\* ( $\text{cm}^{-1}$ ) and their assignment**

[Ni(APAH)Cl] <sub>2</sub> Cl <sub>2</sub>	[Ni(APBH)Cl] <sub>2</sub> Cl <sub>2</sub>	[Ni(BPAH)Cl] <sub>2</sub> Cl <sub>2</sub>	[Ni(BPBH)Cl] <sub>2</sub> Cl <sub>2</sub>	Assignment
3192(3185)	3182(3177)	3184(3180)	3184(3185)	$\nu_{N-H}$
1633(1678)	1627(1654)	1633(1668)	1629(1666)	$\nu_{C=O}$
1578	1600(1616)	1573(1586)	1578(1586)	$\nu_{C=N}$
570	569	597	600	$\nu_{M-O}$
465	481	504	529	$\nu_{M-N}$

\* Spectral bands of ligands are given in parenthesis

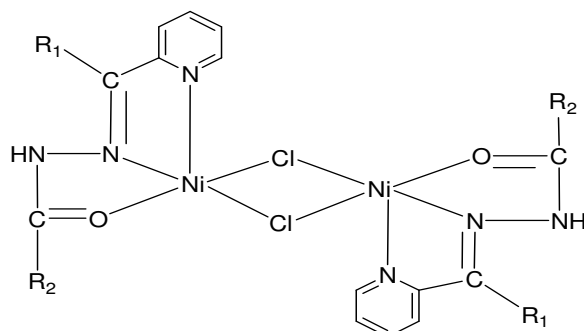
hydrazones act as neutral tridentate ligand in nickel(II) complexes. The non- ligand bands in 569-600 and 465-529  $\text{cm}^{-1}$  regions are

tentatively assigned to  $\nu_{(M-O)}$ , and  $\nu_{(M-N)}$  respectively. Heterocyclic aroylhydrazones are known to react with divalent transition metal

ions and form dinuclear complexes of the general formulae  $[(M HL)_2]X_2$  (Where, HL = heterocyclic arylhydrazone and X = halide) .

Based on physicochemical and spectral data a general structure (Figure 2) for complexes is proposed.

**Figure 2**  
**A proposed general structure for  $[NiLH]_2Cl_2$  complexes**



(Where LH = APAH, APBH, BPAH, BPBH)

$R_1 = CH_3$ ;  $R_2 = CH_3$  APAH

$R_1 = CH_3$ ;  $R_2 = C_6H_5$  APBH

$R_1 = C_6H_5$ ;  $R_2 = CH_3$  BPAH

$R_1 = C_6H_5$ ;  $R_2 = C_6H_5$  BPBH

### Cyclic voltammetric studies

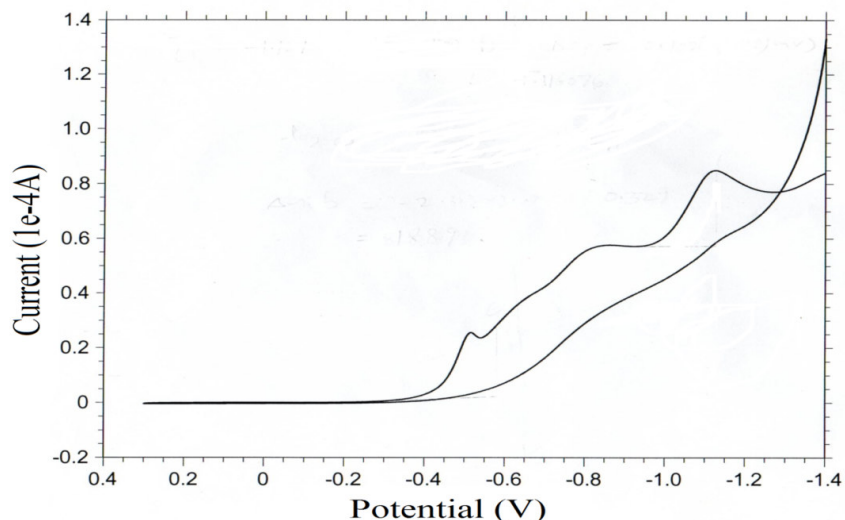
Redox behavior of the nickel(II) complexes have been investigated by cyclic voltammetry in DMF using 0.1M tetrabutylammonium hexafluoro phosphate (TBAHEP) as supporting electrolyte. The cyclic voltammograms of  $[Ni(APAH)Cl]_2Cl_2$  and  $[Ni(BPBH)Cl]_2Cl_2$  complexes show an active response at -1.163 and -1.558V vs Ag/AgCl, assigned to the  $Ni^{II}/Ni^I$  couple (Table 5). The non-equivalent current in cathodic and anodic

peaks for complexes indicate quasi-reversible behavior. The difference  $\Delta E_p = E_{pc} - E_{pa}$  in all the complexes exceeds the Nerstian requirement  $59/n$  mV ( $n$ = number of electrons involved in oxidation reduction) which suggests quasi-reversible character of the electron transfer reaction. The complexes have large separation (85-173 mv) between anodic and cathodic peaks indicating quasi-reversible character.

**Table 5**  
**Cyclic voltammetric data of transition metal complexes**

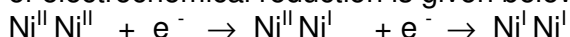
Complex	Redox couple	$E_{pc}$	$E_{pa}$	$\Delta E_p$ (mV)	$E_{1/2}$ (V)
$[Ni(APAH)Cl]_2Cl_2$	II/I	-1.206	-1.121	85	-1.163
$[Ni(APBH)Cl]_2Cl_2$	II/I	-1.68	-1.045	123	-1.106
	II/I	-0.852	-0.724	128	-0.788
$[Ni(BPAH)Cl]_2Cl_2$	II/I	-1.127	-1.025	102	-1.076
	II/I	-0.824	-0.651	173	-0.737
$[Ni(BPBH)Cl]_2Cl_2$	II/I	-1.621	-1.495	126	-1.558

The cyclic voltamograms of  $[Ni(APBH)Cl]_2Cl_2$  and  $[Ni(BPAH)Cl]_2Cl_2$  show two active responses (Figure 4) which are assigned to two one electron reduction steps of in analogy with previous observation<sup>29</sup> for dinuclear complexes.



**Figure 4**  
**Cyclic voltammetric profile of  $[Ni(BPAH)Cl]_2Cl_2$  scan rate at  $25\text{ mVs}^{-1}$**

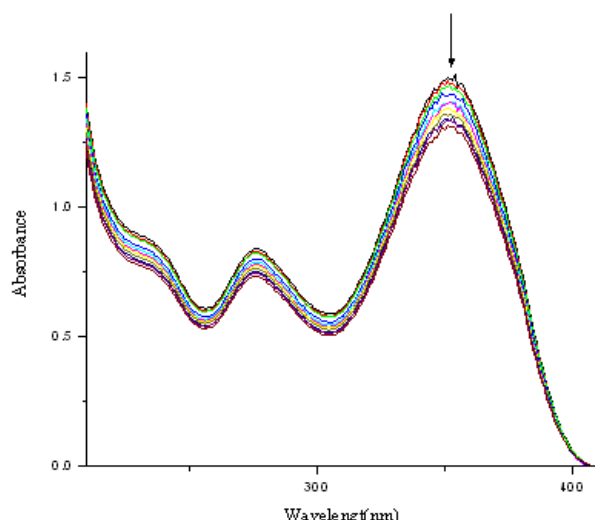
The electrochemical data of metal complexes are presented in Table 5. The possible mechanism of electrochemical reduction is given below.



#### **Electronic absorption titrations**

Electronic absorption spectroscopy is an effective method for examining the interaction of DNA with metal complexes. Hyperchromic and hypochromic effects are the spectral changes when a complex interacts with DNA and forms a new complex. In general, a complex binding with DNA through intercalation usually results in hyperchromism and bathochromism of the absorption band due to the intercalative mode involving a strong  $\pi$ -stacking interaction between the

aromatic chromophore and base pairs of DNA<sup>30</sup>. 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 in 225-370 nm region attributed to  $\pi \rightarrow \pi^*$  transition. Absorption spectra of  $[Ni(APBH)Cl]_2Cl_2$  in the absence and in the presence of CT-DNA are shown Figure 5. The metal-free hydrazone ligands did not show any DNA binding



**Figure: 5**  
**Absorption spectra of  $[Ni(APBH)Cl]_2Cl_2$  in the absence and in the Presence of increasing amounts of CT- DNA.**

activity. The intrinsic binding constants ( $K_b$ ), was determined by using the equation,

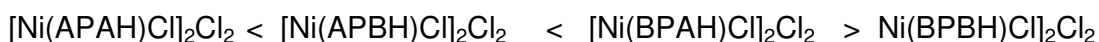
$$[DNA] / (\epsilon_a - \epsilon_f) = [DNA] / (\epsilon_b - \epsilon_f) + 1 / K_b(\epsilon_b - \epsilon_f) \quad \text{-----(1)}$$

Where  $[DNA]$  is the concentration of DNA in base pairs,  $\epsilon_a$ ,  $\epsilon_b$  and  $\epsilon_f$  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  $[DNA] / (\epsilon_a - \epsilon_f)$  versus  $[DNA]$  gave a slope of  $1/(\epsilon_b - \epsilon_f)$ , and vertical intercept equal to  $1 / K_b(\epsilon_b - \epsilon_f)$ ;  $K_b$  was calculated from these values. The data ( Table 6) suggest that the

**Table 6**  
**Electronic absorption data upon addition of CT-DNA to the complexes.**

Complex	$\lambda_{max}$ (nm)		$\Delta\lambda$	H(%)	$K_b$ ( $M^{-1}$ )
	Free	Bound			
$[Ni(APAH)Cl]_2Cl_2$	225	226	1	-5.49	$2.75 \times 10^4$
$[Ni(APBH)Cl]_2Cl_2$	354	353	1	+13.16	$1.46 \times 10^5$
$[Ni(BPAH)Cl]_2Cl_2$	348	347	1	+6.89	$3.12 \times 10^5$
$[Ni(BPBH)Cl]_2Cl_2$	370	374	4	+42.12	$4.51 \times 10^4$

complexes bind DNA strongly. On addition of DNA, the absorbance of the complexes decreases (hypochromism) and absorption maximum is shifted to higher wavelength (bathochromism). These observations suggest that the complexes bind DNA through intercalation involving a strong  $\pi$  - stacking interaction between the aromatic chromophore (pyridine moiety) and base pairs of DNA. The complexes are arranged in the increasing order of binding constants.





The order of binding constants (1) parallels with increasing hydrophobicity of ligand moieties in the complexes. Less binding constant of BPBH complex may be due to its bulky nature. The high binding constants ( $10^4$ -  $10^5$ ) of present complexes, may be attributed to the  $\pi$ - stacking interaction between the aromatic chromophore and base pairs of DNA. Electrostatic attraction between the cationic complex and the negatively charged phosphodiester backbone of DNA may also contribute to the binding constant<sup>31, 32</sup>.

## CONCLUSION

The complexes are characterized based on analytical and spectral data. Higher binding

constants revealed that the complexes bind DNA strongly. The complexes probably bind to DNA via strong supramolecular interactions between the cationic complexes and negatively charged phosphodiester backbone of DNA in addition to hydrophobic interactions.

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