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Synthesis, Characterization, Antimicrobial activity and DNA binding studies of hydrazine complexes of Pyridine-4-carboxylic acid

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Abstract

A new series of hydrazine complexes of transition metal with pyridine -4 carboxylic acid of the formula [M $(Pyc)_2$ $(N_2H_4)_2$] where M = Ni, Co, Cd & Zn and pyc=pyridine -4-carboxylic acid have been prepared and characterized by analytical and physico chemical techniques like IR spectra, UV- visible, CHNS, TG-DTA, VSM and powder XRD studies. The infrared spectral data indicate the bidentate bridging nature of hydrazine molecules. The TG-DTA study of the cobalt complex in air show that, it decomposes steadily to yield metal oxide as residue. The complexes were screened for their antimicrobial activity. DNA binding studies were also carried out for the synthesized complexes. Among the complexes cadmium complex showed higher inhibition against the fungi Candida albicans.

Keywords: (pyc) Pyridine 4- carboxylic acid, Hydrazine, IR spectra, Thermal decomposition, powder XRD, Antimicrobial and DNA binding studies.

Introduction

Hydrazine hydrate was first prepared by Curtius [1] of Germany. Hydrazine hydrate forms salts not only with mineral acids but also with inorganic acids. They include hydrazinium molybdate, selenate, antimonate and hydrazinium metavanadate [2]. Hydrazine forms a number of salts with variety of inorganic acids such as halogen acids [3-5] (HCl, HBr, HI and HF), nitric acid, [6,7], sulphuric [8,9] and perchloric acid [10,11] and are reported by various authors. Hydrazine is an interesting ligand with two free lone pairs of electrons. The possible coordination modes of hydrazine molecule are monodentate, bidentate chelating and also bridging. Hydrazine metal complexes are known with monodentate co-ordination [12-14] and also with bidentate bridging [15-18]. Hydrazine is primarily used as a high energy rocket propellant, as a reactant in military fuel cells, for removal of halogen from waste water, as an oxygen scavenger in boiler feed water to inhibit corrosion and in photographic development [19]. However, historically hydrazine was also used experimentally as a therapeutic agent in the treatment of tuberculosis, sickle cell anemia and non-specific chronic illnesses [20]. There are few reports on the Preparation, characterization and thermal reactivity of divalent transition metal complexes of hydrazine with dinitrogen heterocyclic dicarboxylic acids [21] namely 2-pyrazinecarboxylic acid 3,5-pyrazinedicarboxylic acid [22] and 3,5-dicarboxylic acid, 4,5-imidazole dicarboxylic acid [23]. There are reports for hydrazine metal complexes with divalent metal cations with pyridine 2-carboxylic acid & pyridine 3-carboxylic acid [24] but there is no report on transition metal complexes of hydrazine with pyridine-4-carboxylic acid namely isonicotinic acid. Hence an attempt was made to prepare the complexes of isonicotinic acid with hydrazine as coligand and the results are presented.

Experimental section

Hydrazine metal complexes of pyridine 4-carboxylic acid with hydrazine as coligand was performed and characterized. Transition metals like Ni, Co, Cd and Zn were used for synthesis.

Preparation of the complexes

Prepared M $[(Pyc)_2(N_2H_4)_2]$ complex, where M = Ni, Co, Cd & Zn, Pyc=pyridine-4-carboxylic acid. A requisition quantity of pyridine-4-carboxylic acid (0.2462 g, 0.002 mol) in aqueous medium was stirred with 10% hydrazine hydrate (3.5 ml, 0.007 mol) till a clear solution is obtained. To this ligand solution, metal solution (Ni=0.2908 g, Co=0.2910 g, Zn=0.297 g, Cd=0.3084 g, 0.001 mol) was added drop wise with constant stirring. After stirring the solution was concentrated on a water bath. A polycrystalline substance obtained after the addition of metal solution was washed with distilled ethanol, and dried in desiccators. The hydrazine content in the sample was determined by estimation using KIO_3 as the titrant. The % of metal in the sample was estimated by standard methods given in the VOGEL’S text book [25].

Results and discussion

The analytical data of the complexes coincide with the proposed composition for the complexes and the results are presented in (table1)

Table 1-Analytical Data

Compound	Colour	Hydrazine %		Metal %		Melting point (°C)
		Found	Calculated	Found	Calculated	
$Ni[(Pyc)_2(N_2H_4)_2]$	Light violet	17.70	17.35	15.60	15.90	332
$Co[(Pyc)_2(N_2H_4)_2]$	Light orange	17.33	17.34	15.55	15.95	330
$Zn[(Pyc)_2(N_2H_4)_2]$	Dull White	16.65	17.03	17.70	17.40	346
$Cd[(Pyc)_2(N_2H_4)_2].H_2O$	Pale yellow	14.52	14.52	25.51	25.47	352

Infrared spectral data in (cm^{-1})

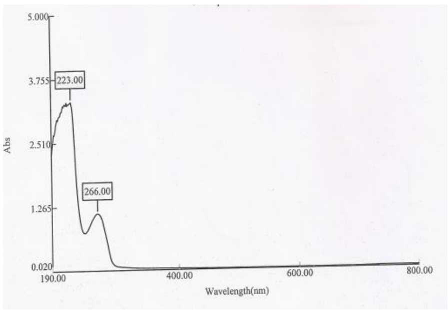
Infrared spectra were recorded on IR-Affinity-1 CE-Shimadzu model spectrometer. The chemical composition of complex is M $[(pyc)_2(N_2H_4)_2]$ for M=(Ni, Co, and Zn) and $M[(pyc)_2(N_2H_4)_2.H_2O]$ for M=Cd. The OH stretching frequency of cadmium complex appears at 3483 cm^{-1}confirming the presence of water molecule in the complex. The infrared spectra showed bands in the region at 3203-3309 cm^{-1} for N-H stretching. The asymmetric and symmetric stretching frequencies of carboxylate ions are shown at 1726-1741cm^{-1} and 1588-1620 cm^{-1}. The N-N stretching frequencies appear in the range 954- 980 cm^{-1} [26-28] which helps to confirm the bidentate bridging nature of hydrazine ligand. The important infrared spectral data of all the complexes with their band assignments are summarized in the (table 2)

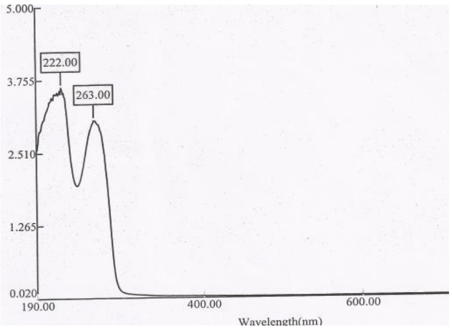
Table 2

Compound	ν (O-H)	ν (N-H)	ν asym (COO^-)	ν sym (COO^-)	ν (N-N)
$Ni[(Pyc)_2(N_2H_4)_2]$	-	3297	1726	1620	980
$Co[(Pyc)_2(N_2H_4)_2]$	-	3203	1741	1588	954
$Zn[(Pyc)_2(N_2H_4)_2]$	-	3295	1741	1606	975
$Cd[(Pyc)_2(N_2H_4)_2].H_2O$	3483	3309	1738	1589	962

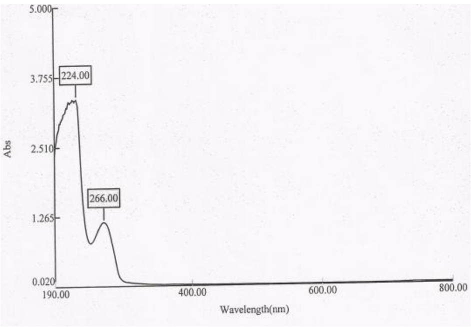
Electronic spectra

The electronic spectra of the complexes were recorded in $CHCl_3$ in the region 190-800 nm bands appear at 222nm and 226nm which are assigned to $A_{2g}{}^3(F)$ - ${}^3T_{1g}$ (p) transition, characteristic of octahedral geometry of metal ions.





UV Spectra of Cobalt complex **UV Spectra of Zinc complex**



UV Spectra of Cadmium complex

Elemental analysis

Elemental analysis was performed on vario EL III CHNS analyser.

Elemental analysis data of the complexes are listed in table (3). The percentage of CHN in the complexes matched with the found CHN analysis.

Table 3 Elemental analysis

Complexes	%C		%H		%N	
	Found	**Calcd**	**Found**	**Calcd**	**Found**	**Calcd**
$Ni[(Pyc)_2 (N_2H_4)_2]$	39.02	39.07	4.90	4.91	22.66	22.77
$Co[(Pyc)_2(N_2H_4)_2]$	39.00	39.04	4.86	4.97	22.67	22.76
$Zn[(Pyc)_2(N_2H_4)_2]$	38.34	38.36	4.27	4.29	23.34	22.36
$Cd[(Pyc)_2(N_2H_4)_2].H_2O$	32.68	32.70	4.44	4.50	19.01	19.06

Thermal analysis

The TG-DTA was recorded on perkin-Elmer SII thermal analyzer. The TG-DTA of the Co complex are presented in the figure (I)

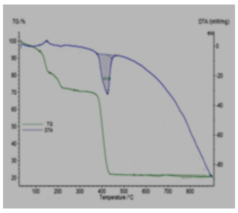


Figure I

TG-DTA of the Co complex

The TG-DTA data of the cobalt complex is summarized in table (4).

Table 4

Complex	DTA peak Temp(^{O}C)	Thermogravimetry			Nature of decomposition
		Temp Range (^{O}C)	Mass loss (%)		
			Found	Calculated	
Co[(Pyc)$_2$(N$_2$H$_4$)$_2$]	148(-)	50-200	17.72	17.34	Dehydrazination
	424(+)	200-450	49.64	49.91	Complete decomposition leading to metal oxide residue.

(-) exothermic, (+) endothermic.

Magnetic studies

Cobalt and nickel complexes were subjected to VSM studies (vibrational sample magnetometer) in the field of -10000 to 20000 gauss. The analysis confirmed the paramagnetic nature of metals in the complexes. M [(pyc)$_2$ (N$_2$H$_4$)$_2$ VSM studies shown in the figures (II & III).

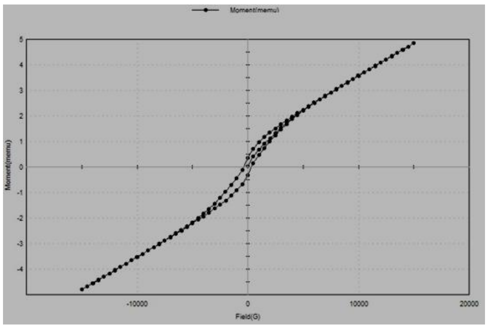


Figure II VSM of Nickle complex

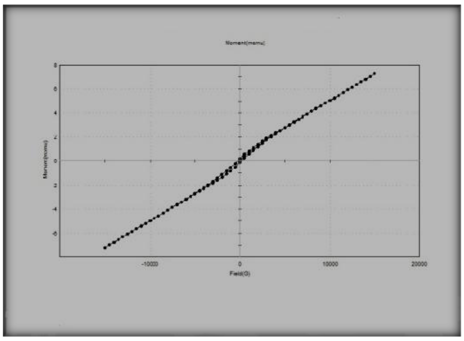


Figure III VSM of Cobalt complex

X-ray diffraction studies

X-ray diffraction studies were performed on a Bruker Advanced D8 X-ray diffractometer.

The XRD patterns of the complexes are presented in the figure (IV). All the complexes show almost similar powder XRD patterns showing that the all complexes are isostructural in nature.

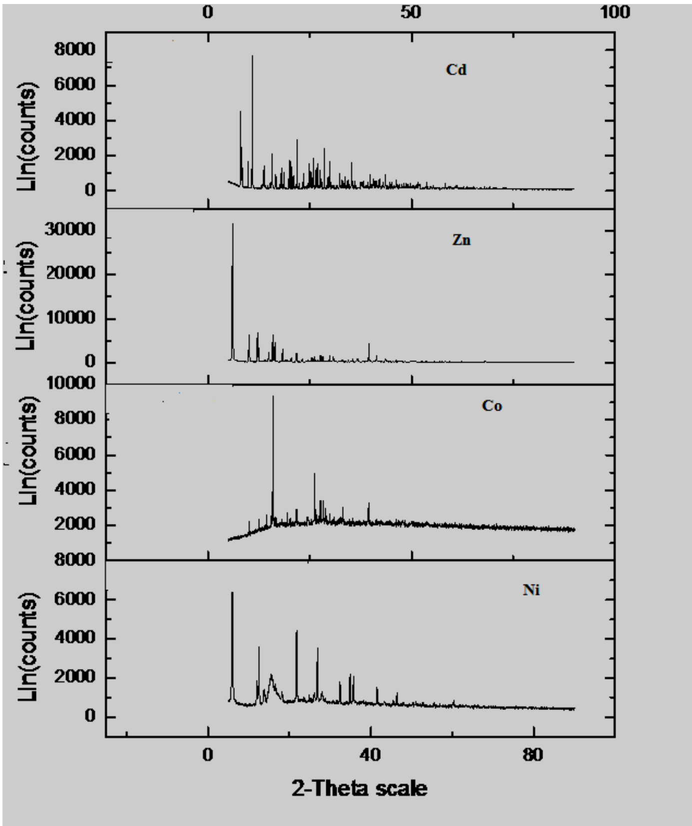


Figure IV X-ray powder diffraction pattern of Ni, Co, Zn and Cd complexes

Antimicrobial Studies

Antimicrobial studies were performed by disc diffusion method. The complexes were screened in vitro for their growth inhibitory activity against the pathogenic bacteria E.coli, Stapylococcus aureus and fungi Candida albicans and Aspergillus fumigates. The inhibition zones (in mm) and MIC of the complexes are given in table 5 and 6. All the complexes possess antibacterial and antifungal activity.

Antibacterial activity shown in the table (5) and figure (V). Studies indicates that the cobalt complex has more bacterial activity compared to other complexes against E.coli and Staphylococcus aureus. MIC of Co and Zn complexes are tabulated in the table (7 & 8).

Table 5 Antibacterial activity data for the complexes.

S.no	Complexes	Zone of Inhibition (mm)	
		E.coli	Stapylococcus Aureus
	McFarland Standard	30	33
1	Ni[(Pyc)$_2$(N$_2$H$_4$)$_2$]	09	08
2	Co[(Pyc)$_2$(N$_2$H$_4$)$_2$]	13	12
3	Zn[(Pyc)$_2$(N$_2$H$_4$)$_2$]	09	09
4	Cd[(Pyc)$_2$(N$_2$H$_4$)$_2$]	10	10

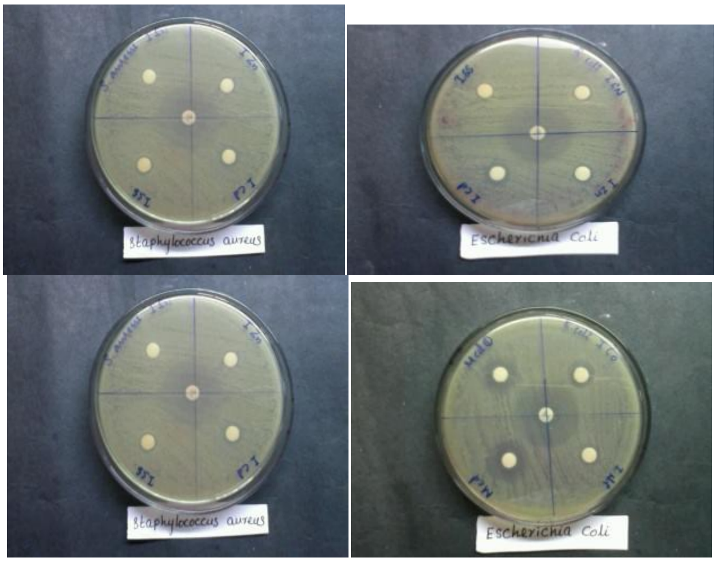


Figure V Ni, Co, Zn & Cd complexes against Stapylococcus aureus and E.coli

This studies exhibit that zinc and cadmium hydrazine complex has more antifungal activity compared to other complexes against Aspergillus fumigates and Candida albicans.

Table 6 Antifungal data of the complexes

s.no	Complexes	Zone of Inhibition (mm)	
		Candida albicans	**Aspergillus fumigates**
	McFarland Standard	13	12
1	Ni[$(Pyc)_2$ $(N_2H_4)_2$]	08	08
2	Co[$(Pyc)_2(N_2H_4)_2$]	08	08
3	Zn[$(Pyc)_2(N_2H_4)_2$]	19	07
4	Cd[$(Pyc)_2(N_2H_4)_2$].H_2O	19	07

Table 7 MIC data of the Co complex against E.coli bacteria

Complex	Organisms	1000 µg/ml	500 µg/ml	250 µg/ml	125 µg/ml	62.5 µg/ml	31.25 µg/ml	15.625 µg/ml
Co[$(Pyc)_2(N_2H_4)_2$]	E.coli	-	-	-	-	-	+	+

Complex	Organisms	MIC value
Co[$(Pyc)_2(N_2H_4)_2$]	E.coli	62.5µg/ml

\+ → Presence of Growth

\- → Absence of Growth

The complexes possess antimicrobial activity. Among the synthesized complexes Co complex were found to be more active against E.coli bacteria. Minimum inhibitory concentrations study the synthesized compound Co having greatest value 62.55 mg/ml.

Table 8 MIC data of the Zn complex against Candida albicans

Complex	Organism	1000 µg/ml	500 µg/ml	250 µg/ml	125 µg/ml	62.5 µg/ml	31.25 µg/ml	15.625 µg/ml
Zn[$(Pyc)_2(N_2H_4)_2$]	Candida Albicans	-	-	-	-	+	+	+

Complex	Organisms	MIC value
Zn[$(Pyc)_2(N_2H_4)_2$]	Candida albicans	125µg/ml

\+ → Presence of Growth - → Absence of Growth

The anti microbial activity study confirms that the complexes possess antimicrobial activity. Among the synthesized complexes Zn complex were found to be more active against Candida albicans fungi. Minimum inhibitory concentrations study for the Zn complex has the greatest value of 125µg/m.

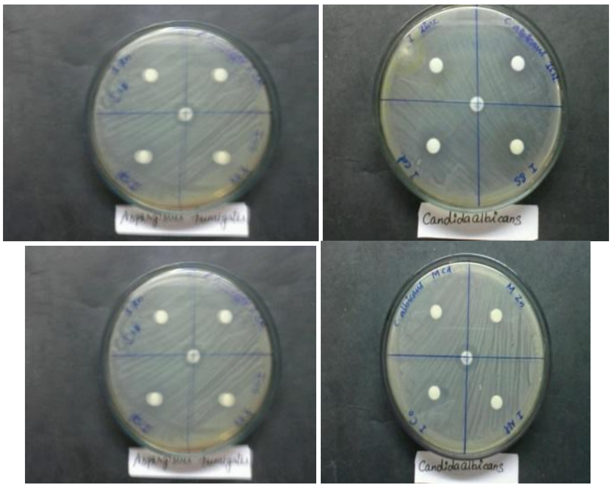


Figure VI Ni, Co, Zn & Cd complexes against Candida albicans and Aspergillus fumigates

DNA binding study

Protocol

The extracted cough thymus DNA of 10 µl was added with metal solution each 10 µl and incubated at 37° C for 3 hours. The control was DNA and distilled water. It was then run on horizontal agarose gel electrophoresis in 0.8 % agarose slab gel in 1X Tris- Acetate EDTA (TAE) buffer at room temperature. The 6X gel loading dye was added to the DNA-metal mixture and control which in turn was loaded on the gel 15 µl and the electrophoresis unit was run at 50 V with an appropriate DNA marker till the dye migrated to a sufficient distance in the gel and visualized using a UV trans illuminator.

UV-Vis spectrophotometric studies

To the 10 mg of Deoxyribonucleic acid, 1 ml of sterile distilled water and 50 µl of each cobalt and nickel solution was added and incubated at room temperature for an hour. The controlled was maintained without adding the metals. The samples were measured at 370 nm in UV-vis spectrophotometer and readings were measured The metals complexes were mixed with calf thymus DNA and incubated for 3 hrs in room temperature and run on 0.8% Agarose gel and the results were viewed under gel documentation and documented. The presence of DNA bands denoted the binding of the compounds with the test DNA [29]. Figure (VI) shows the DNA binding ability of the complex.

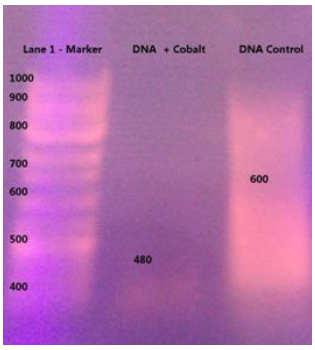
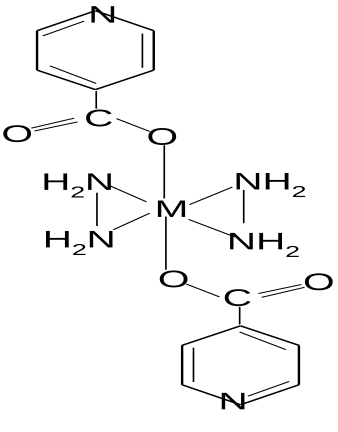


Figure VI DNA binding study of Cobalt complex

Conclusion

It is found that the reaction of metal nitrates with hydrazine in the presence of pyridine -4 carboxylic acid, at pH 7 yields neutral hydrazine complexes. During heating, all complexes undergo similar type of decomposition through their metal carboxylate intermediates to give their corresponding metal oxides as residue. Based on the physical nature of the complexes formed, which are powdery, insoluble in any medium, and also from the evidences drawn from IR, TG-DTA, CHNS, UV, powder XRD and VSM studies a six coordination with octahedral geometry is proposed for the complexes. Hydrazine acts as the bridging bidentate ligand, pyridine-4-carboxylates acts as monodentate ligand with the carboxylate ion co-ordinating to the metal. The following structure was assigned for the complexes. The new complexes have been found to possess DNA-binding abilities.



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