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Biological activity of bis(nicotinohydroxamato) oxidovanadium(IV) complex

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ABSTRACT

The oxidovanadium(IV) hydroxamate complex of composition [VO($C_5H_4NCONHO)_2$] has been synthesized by the reaction of $VOSO_4.5H_2O$ with two equivalents of potassium salts of nicotinohydroxamic acid in aqueous methanol medium. The complex has been characterized by elemental analyses, molar conductivity, magnetic moment measurements, electrochemical and IR, UV-Vis spectral and mass spectrometric studies. Based upon spectral studies, a square-pyramidal geometry around vanadium has tentatively been proposed for complex. The antimicrobial potential of complex has been assayed against some pathogenic bacteria E. coli, S. aureus, S. typhi, S. paratyphi, S. epidermidis, K. pneumoniae and fungi C. albicans, B. fulva and F. oxysporum by minimum inhibitory concentration method. The complex has been found to possess promising antimicrobial potential relative to ligands. Thermal behavior of complex has been studied by TG-DTA techniques. The coordination compounds of complex with 2-cyanopyridine and 4-aminobenzonitrile have also been synthesized and characterized by physicochemical and IR spectral technique. Cytotoxicity of complex was assayed on mammalian transformed cell line Hep2c, by MTT assay.

Keywords: Oxidovanadium(IV) complexes, Antimicrobial activities, Nicotinohydroxamic acid.

INTRODUCTION

Over the years an ever increasing research interest in the chemistry of vanadium has been aroused due to the tendency of vanadium to exhibit a range of oxidation states [1], affinity for a variety of ligands, structural novelties, complexities and physiological effects [2]. The potential applications of vanadium complexes as pharmacological agents [3-5] antimicrobial [6-7], anticancer [8] catalytic activities [9], in organic synthesis and material science [10-11] have drawn the special attention of inorganic chemists.

Of a variety of biologically important ligands known to form metal complexes, hydroxamic acids having RCONHOH group, constitute an important class of organic bioligands [12-13]. The hydroxamic acid moiety is a constituent of antibiotics, antifungal agents, food additives, drugs, tumor inhibitors and growth factors [14-16]. The derivatives of hydroxamic acid are biochemically highly active and find applications in medicinal use [17-20] and have nitric oxide-releasing properties [21]. The reactivity of hydroxamic acids towards nucleic acids and sulfhidryl groups of proteins has been established to be the reason for their inhibitory effect on various enzymes. The chemistry of vanadium hydroxamate interactions is of significance because of there use as bioinorganic model compounds [22].

A particular interest in selection of ligand nicotinohydroxamate used in present work stems from the fact that cinnamic acid derivatives are known to exhibit various biological and pharmacological activities viz. antioxidant, nicotino hydroxamate finds use as an active component in the inhibition of melanogenesis [23]. As a part of our continuing research interest on oxovanadium (IV) and nonoxovanadium(IV) hydroxamate complexes [24] we report herein the synthesis and structural characterization of oxidovanadium(IV) hydroxamate complex derived from

nicotinohydroxamate ligands (Fig. 1,2) of biological relevance [25-27]. The newly synthesized complex has been assayed for their biological activity.

MATERIALS AND METHODS

All the solvents used were of A.R. grade and were distilled and dried, prior to use, by standard methods. Vanadyl sulphate ($VOSO_4.5H_2O$) (Merck) was used as procured. The potassium nicotinohydroxamate (KHL) was synthesized by reported method [28] and characterized by microanalysis and IR spectra while vanadium content in the complex was determined gravimetrically as V_2O_5 and C, H and N analyses were obtained on an Carlo-Erba elemental analyser. The molar conductance measurement of (10^{-3} $molL^{-1}$ solutions in methanol) were made on an Elico conductivity bridge type CM-82T. FTIR spectra of complexes were collected on a Nicolet-5700 FTIR spectrophotometer (4000-200 cm^{-1}) using KBr pellet and pellet was prepared in a dry box to avoid moisture. The room temperature magnetic susceptibilities were measured by Gouy's method using $Hg[Co(NCS)_4]$ as calibrant. Electronic spectra of complex was recorded on a Varian Cary-100 Bio UV-Vis. spectrophotometer using methanol as solvent. The mass spectra of complex was recorded at room temperature as electron spray mass spectrometry. The electrochemical study was carried out on CH instrument electrochemical analyzer. All voltammetery experiments were performed in single compartmental cell of volume 10-15ml containing a three–electrode system comprising of Pt-disk working electrode, Pt-wire as auxiliary electrode and an Ag/AgCl electrode as reference electrode in MeOH + H_2O (95:5) medium with Bu_4NClO_4 as supporting electrolyte. The potentials was measured against Ag/AgCl reference electrode. Thermograms of complex was recorded on EXSTAR TG/DTA 6300 at a heating rate of 10 ^0C min^{-1} in nitrogen atmosphere.

Synthesis

Preparation of $[VO(C_5H_4NCONHO)_2]$

In a typical reaction, to a solution of $VOSO_4.5H_2O$, (0.5g, 1.95 mmol) in aqueous methanol (20mL), a solution of KHL (0.7g 3.97 mmol) in methanol was added. The reaction mixture was stirred for 1h. The concentrate was then dried under vacuum by repeatedly treating with petroleum ether whereupon dark brown solid was obtained. The concentrate was then filtered and residue was purified from dichloromethane.

Anal. Calcd for $VC_{12}H_{10}O_5N_4$ (341) C, 42.28; H, 2.93; N, 16.42; V, 14.95. Found (%) C, 42.32; H, 2.97; N, 16.47; V, 14.97. Λ_m ($PhNO_2$):9.79 Scm^2mol^{-1}; μ_{eff} (293K): 1.70 B.M. (Yield: 1.14g, 85%).

Preparation of Coordination compounds of $[VO(C_5H_4NCONHO)_2]$ with 2-cynopyridine and 4-aminobenzonitrile

To a methanolic solution of $[VO(C_5H_4NCONHO)_2]$, equimolar amount of 2-cynopyridine and 4-aminobenzonitrile were added in separate experiments. The reaction mixture was stirred for 4 h at room temperature during which separation of black color solid was observed. The solid compounds so obtained were treated with petroleum ether and finally dried under vacuum. Anal. Calcd. for $C_{18}H_{12}N_6O_5V$ (Formula weight, 443) (%) : C, 48.75; H, 2.70; N, 18.96; V, 11.56. Found: C, 48.79; H, 2.75; N, 18.98; V, 11.56 Λ_m =9.79 Scm^2mol^{-1}; μ_{eff} ; 1.76 B.M.. Anal. Calcd. For $C_{19}H_{14}N_6O_5V$ (Formula weight, 457) (%): C, 49.89; H, 3.06; N, 18.38; V, 11.16. Found: C, 49.93; H, 3.09; N, 18.43; V, 11.19; Λ_m =9.50 Scm^2mol^{-1}; μ_{eff} ; 1.70 B.M..

Antimicrobial activity Test

The *in vitro* antibacterial and antifungal activity of oxidovanadium(IV) hydroxamate complex was studied against fungi and bacteria viz. Gram (+ve) and Gram (-ve)) by a minimum inhibitory concentration (MIC) method [29-30]. MIC is the lowest concentration of the antimicrobial agents that prevents visible growth after overnight incubation. The samples were tested in triplicate. All the test cultures were streaked on soya bean casein agar (SCDA) and incubated overnight at 37 ^0C. The MIC assay was performed in a 96-well microlitre plate. For MIC assay of each drug, a row of 12 wells was used out of which last two wells were taken as control (no drug added). Each of the ten wells received 100µL of the Muller-Hinton broth, except the first well that received 200 µL of broth containing 500 µg mL^{-1} concentration of the test drug. From the first well (containing test drug), 100 µL broth was withdrawn with a sterile tip and added to the 100 µL of the broth in the second well and contents were mixed four times. Then 100 µL was withdrawn from second well and was added to the third well. In this way a range of two-fold serial dilutions were prepared (500-0.98µgmL^{-1}) in DMSO. The broth in each well was inoculated with 2µL of the bacterial culture and the contents were mixed by 10 clockwise and 10 anticlockwise rotations on flat surface. The plate was incubated at 35^0C thereafter and observations for growth of bacteria were recorded after 24h.

Cell culture. Human Cervix carcinoma (HeLa) cells were trypsinized from a confluent monolayer culture obtained in a 25 cm^2 canted neck flask. The confluent monolayer of the cells was washed twice with phosphate-buffer saline (PBS), pH 7.2 followed by with exposure to Trypsin-EDTA (100 mg % EDTA and 125 mg % Trypsin 1:250;

Sigma Chemical Co. St. Louis, USA) disaggregating solution for two minutes. The disaggregating solution was completely removed by decantation and the enzyme solution treated flask was incubated at 37 ^{0}C for three minutes. The disaggregated cells were resuspended in appropriate volume of Dulbecco's modified Eagels's medium (DMEM) supplemented with fetal calf serum (FCS) (10%, v/V) and adjusted to a cell density of 4×10^3 cells/mL.

In Vitro Cytotoxicity Assay. The uniform volume of Hep2C cell suspension (200 µL/well) was poured in the selected wells of a 96-wells tissue culture plate. The columns were marked, in wells under each of the columns the filter sterilized drug compound prepared in DMSO (0.1 M stock) was dispensed to achieve final concentration of 2, 4, 8, 20 and 28 mM. The cells treated with drug compound were incubated in a CO_2 incubator with 95% humidity at 37^{o}C for 16-18h. The drug compound concentrations were tested in quadruplicate and mean values were calculated after MTT assay (using 5mg mL^{-1} in PBS, 0.1 M pH 7.2 of MTT (1-(4,5-dimethyl-thiazol-2-yl)-3,5-diphenylformazan) compound. The appropriate controls with no drug compound but containing appropriate amount of DMSO (used to prepare stock of drug compounds) were also incubated to see if DMSO alone has any effect on the viability of the proliferating cells cultured in vitro.

RESULTS AND DISCUSSION

The interaction of $VOSO_4.5H_2O$ with bimolar amount of nicotinohydroxamate (fig. 1) in aqueous methanol solvent medium leads to the quantitative formation of complexes in agreement with elemental analyses. The reaction can be rationalized as:

$$VOSO_4\cdot 5H_2O \xrightarrow{2(C_5H_4NCONHOK)} VO(C_5H_4NCONHO)_2 + K_2SO_4 + 5H_2O$$

Scheme1. Synthesis of bis(hydroxamato) oxidovanadium(IV) complex

The complex is dark brown fine powders soluble in DMSO and methanol. The molar conductance values of (10^{-3} M solutions) in methanol was 1.0 S cm^2 mole^{-1} suggested non electrolytic nature of complex. The cryoscopic molecular weight determinations of complexes in nitrobenzene indicated these to exist as monomers in this solvent. The room temperature magnetic moment value of complex was 1.79 μ_B respectively are in confirmation with their paramagnetic nature and +4 oxidation state for vanadium. The vanadium content in the complex was determined gravimetrically as V_2O_5.

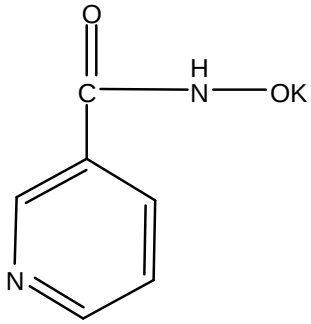


Fig. 1

IR Spectra

The formation of complex has been inferred from a comparison of their IR spectra with those of free hydroxamate ligand, scanned in 4000-200 cm^{-1} region. The characteristic bands of hydroxamic group are due to υ(C=O), υ(C–N), υ(N–O) and υ(N–H) modes which undergo significant change on complexation. The KHL displayed bands at 1620, 1353, 1015 and 3104 cm^{-1} due to υ(C=O), υ(C–N), υ(N-O) and υ(N–H) modes. These bands appeared at 1525, 1467, 1000 and 3110 cm^{-1} respectively in complex $VO(C_5H_4NCONHO)_2$. A shift in υ(C=O) mode to lower wave number and υ(N–H) mode remains almost unshifted in the complex suggested the bonding through carbonyl and hydroxyl amine oxygens in oxidovanadium(IV) complex [31]. The absorption band due to υ(C–N) mode occurring at 1353 cm^{-1} in KHL has been found to shift to higher region at 1467 cm^{-1} in complex. It is important to mention here that in complexes of cobalt(II) and nickel(II) with nicotinnohydroxamic acid bonding occur through nitrogen and (NO) coordination have been indicated [32-33]. Absorption bands appeared at 978 cm^{-1} is due to υ (V=O) mode. The non-observance of bands at 785 cm^{-1} assignable to υ (V-O-V) asymmetric stretch are indicative of mononuclear nature of complex.

Mass Spectra

The mass spectra of complex showed molecular ion peaks confining the profound formula. The mass spectral results along with elemental analysis agree with formation of complexes.

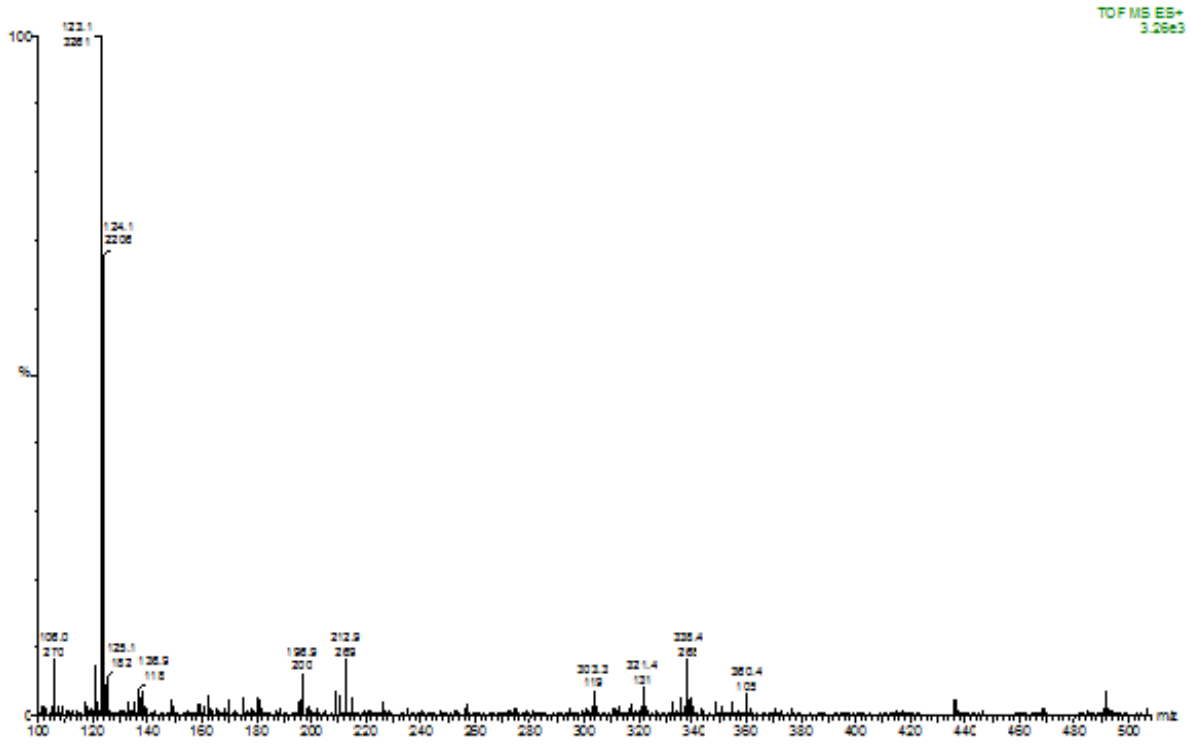


Fig. 2 Mass spectra of Bis(hydroxamato) oxidovanadium(IV) complex

Oxidovanadium (IV) complex $[VO(C_5H_4NCONHO)_2]$ display molecular ion peak at m/z 338 respectively (table 1). Complex showed base peak at m/z 123 corresponding to $[HL\text{-}O+2H]^+$. The other fragment ions appeared at m/z 338(8.21), 321(4.01), 303(3.64),137(3.61), 123(100), 106(8.27) (Fig. 2) corresponds to $[VO(HL)_2\text{-}O+4H]^+$, $[VO(HL)_2\text{-}2OH\text{-}4H]^+$, $[HL]^+$, $[HL\text{-}NHO]^+$ respectively.

Table 1: Mass spectra of bis(hydroxamato) oxidovanadium(IV) complex

Complex	m/Z
$VO(HL^2)_2\text{-}3H]^+$	338(8.21)
$[VO(HL^2)_2\text{-}O+4H]^+$	321(4.01)
$[VO(HL^2)_2\text{-}2OH\text{-}4H]^+$	303(3.64)
$[HL^2]^+$	137(3.61)
$[HL^2\text{-}O+2H]^+$	123(100)
$[HL^2\text{-}NHO]^+$	106(8.27

Electrochemical studies

Vanadium exhibits different oxidation states, the reduction/ oxidation is known to occur between different oxidation states without any role played by the ligands. In order to probe the electronics of ligand binding and redox properties, the electrochemical studies of oxidovanadium (IV) complexes by cyclic Voltammetery (table 2) has been performed. A negative scan was initiated in positive direction at different scan rates 0.001 V/s – 0.0025 V/s in MeOH + H_2O (95:5) with Bu_4NClO_4 as supporting electrolyte. A blank CV run with the ligands in the potential range -2.0 to +2.0 gave one peak at +1.0 due to oxidation of the ligands. The non observance of this peak in complexes suggested that the redox process is metal centered only. Cyclic voltammogram of complex was performed at different scan rate.

Table 2: Cyclic voltammetric data for bis(nicotinohydroxamato)oxidovanadium(IV) Complex

Complex	Scan rate mV/s	Redox couple	Epa(V)	Epc (V)	ΔE (mV) $Ep_a\text{-}Ep_c$	Ipa	Ipc	Ipa/Ipc	nΔE
$[VO(HL)_2$	100	VO^{IV}/V^{III}	-	-0.5987	-	-	-6.7667	-	-
$[VO(HL)_2$	150	VO^{IV}/V^{III}	-	-0.6966	-	-	1.42	-	-
$[VO(HL)_2$	200	VO^{IV}/V^{III}	-	-0.8886	-	-	2.54	-	-
$[VO(HL)_2$	250	$VO^{IV}/VO^{V}/V^{III}$	-0.7035	-0.4563	24.72	-1..60	3.53	0.45	58.77

The Voltammogram at different scan rate of 100, 150, 200 mV/s for complex of composition $VO(C_5H_4NCONHO)_2$ depicted only cathodic peak and no anodic peak has been observed. However at scan rate of 250 mV/s there is

feeble anodic peak and significant cathodic peak. An explanation for significant cathodic peak at different scan rates and absence of anodic peak may be assigned to be the presence of lone pair of electrons on nitrogen of pyridine ring which contribute to reduction of vanadium metal. The absence of anodic peak in this complex is indicative of its stability towards oxidation [34-35]. The general electrode process can be represented by following equations:

$$V^{IV} \rightleftharpoons V^{V} + e^{-1} \quad (1)$$

$$V^{IV} + e^{-1} \rightleftharpoons V^{III} \quad (2)$$

Thermal Studies

The thermal decomposition behavior of hydroxamato oxidovanadium (IV) complex $VO(C_5H_4NCONHO)_2$ has been studied by thermogravimetric and differential thermal analysis techniques in N_2 atmosphere [fig. 3]. The thermal data of complex is presented in table 3. The TG curve of complex has shown that complex is thermally stable upto 78 ^{0}C respectively after which temperature complexes undergo decomposition in continuous single step.

Table 3: Thermal decomposition data of bis(nicotinohydroxamato)oxidovanadium(IV) Complex

Complex	Initial decomposition temperature (^{0}C)	Stages of decomposition (^{0}C)	TGA Data			DTA Data	
			Decomposition Range	Weight loss (%)	Decompositio Products	Peak temperature	Peak nature
$VO(HL)_2$	78	Single	78-474 (^{0}C)	42	$VO(HL)_2$-2HL	190 465	Exothermic (Feeble) Exothermic (Feeble)

The complex of composition $VO(C_5H_4NCONHO)_2$ TG-DTA chart show that complex is stable up to the temperature 100^{0}C after which it undergo single step decomposition with wt. loss of 42.8% with dark color residue corresponded to formation of $VO(C_5H_4NCONHO)$ as the product of decomposition. The complex display two exothermic peaks 190 ^{0}C, 465 ^{0}C in DTA curves.

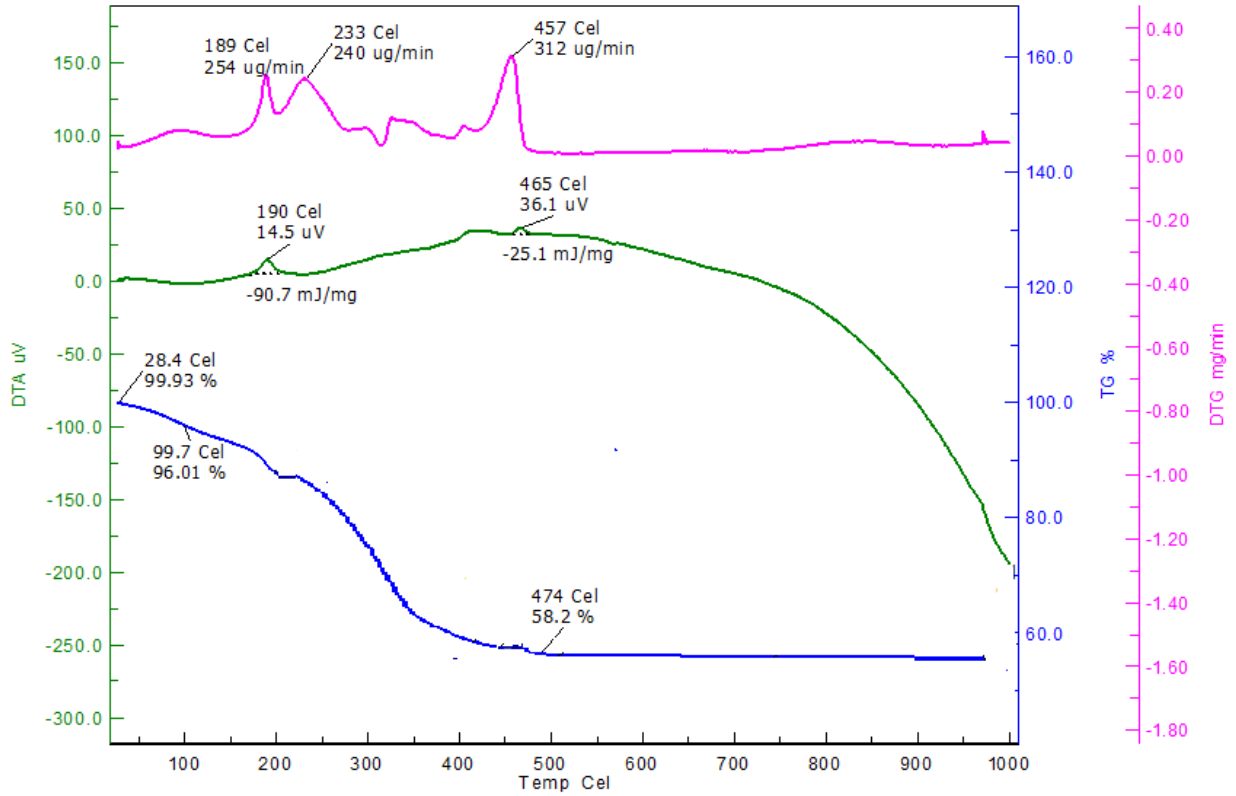


Fig 3. TG-DTA graph of Bis(hydroxamato) oxidovanadium(IV) complex

$$VO(C_5H_5NCONHO)_2 \longrightarrow VO(C_5H_5NCONHO) \quad (5)$$

Electronic absorption spectra

The UV/Vis spectra of ligands and complex has been recorded in methanol. The Uv/Vis spectra of $VOSO_4.5H_2O$ exhibits bands at 252, 306, 780 nm in consonance with most of vanadyl complexes [36]. The free ligand displayed absorption bands at 246, 258 nm and 262, 292, 348 nm respectively. Complexes $VO(C_5H_4NCONHO)_2$ exhibited bands at 386(1175), 422(678), 580(140), 710(42) nm and 364 (1187), 458(668), 574(149), 718 (30) nm respectively. The intense high energy bands appearing at 364 nm in complex (I) may be assigned metal ion induced charge transfer transition. The less intense absorption bands appeared at 574 nm may be ascribed to ^2Eg-$^2T_{2g}$ transition characteristic of oxidovanadium(IV) coordinating to good π donating ligands. The absorption bands at 458 nm may be assigned to LMCT transition originating from lone pair of electrons on oxygen atom of hydroxamate ligands into an empty d orbital of the vanadium ion. The absorption bands observed at 718 nm may be assigned to be originating from a lone pair of p orbitals on the hydroxamate ligand (π) into an empty d orbital of vanadium to induce strong charge transfer to the metal center in complexes with high valence metal ions. On the basis of IR, electronic and mass spectral data, a square pyramidal geometry for the complex has tentatively been proposed (Fig. 4).

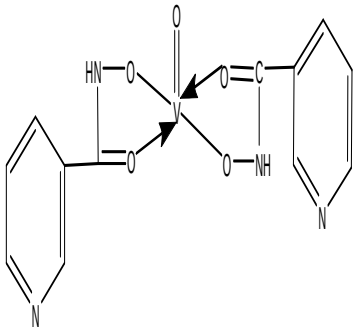


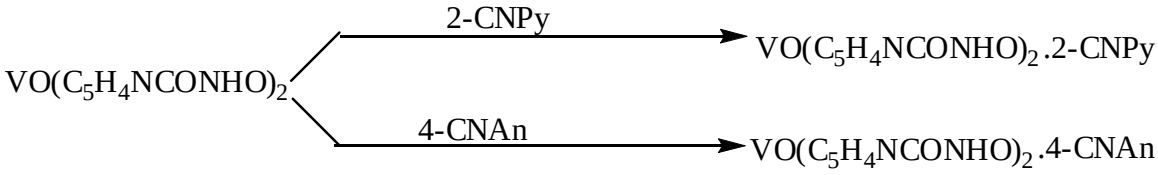
Fig. 4 Geometry of bis(nicotinohydroxamato)oxidovanadium(IV) complex

Magnetic studies

The room temperature solid state magnetic moment values of 1.75 B.M. corresponds to the spin only value , S=1/2 for $[VO(HL)_2]$ establishing, thereby the mononuclear and paramagnetic nature of complex.

Reactions with nitrogenous bases

Literature contains scattered reports on the reactivity of cyanopyridine (CNPy) and cyanoanilines (CNAn) towards various metal halides and complexes, to study their binding modes/coordination sites. The interactions of $VO(C_5H_4NCONHO)_2$ with equimolar amounts of 2-cyanopyridine and 4-cyanoanniline in methanol leads to the formation of 1:1 coordination compounds according to the scheme 2:

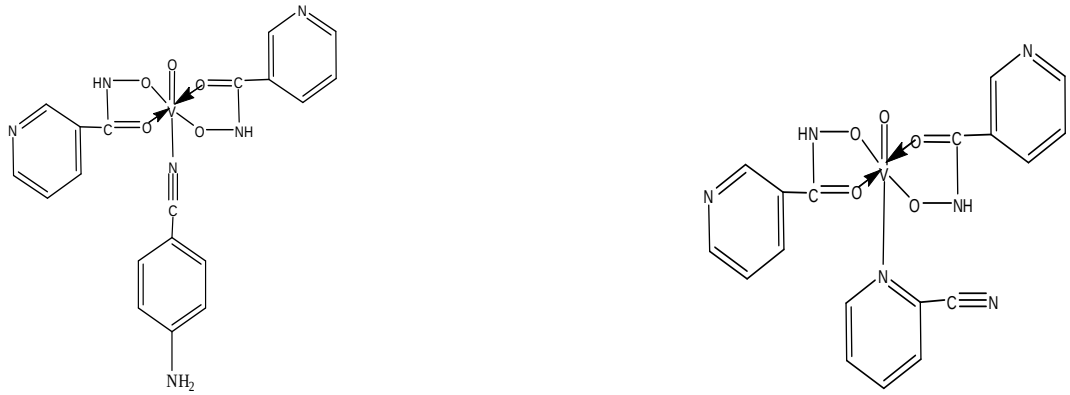


Scheme 2: Addition compound of Bis(nicotinohydroxamato) oxidovanadium(IV) complex

Information on the structure of these adducts has been obtained from their IR spectra as it plays a key role in deciding the bonding mode of ligands. The cyanoanilines possessing two potential donor sites ($-NH_2$ and –CN), have been reported to behave as monodentate or bidentate depending upon as to whether the coordination takes place through $–NH_2$/-CN group or both. The coordination through nitrile group is known to result in an increase in ν(CN) mode [37] while coordination through $–NH_2$ gp. results in shift of this mode to lower wave numbers. Also a decrease in ν(CN) mode considered to result from coordination of cyano group through its triple bond [38-39]. In the IR spectra of the coordination compound of $VO(C_5H_4NCONHO)_2$ with 4-CNAn, the bands due to ν_{asym} NH and ν_{sym} NH vibrations occurring at 3442 and 3360 cm^{-1} have been observed to remain almost unaltered, suggesting that amino group is not involved in coordination to metal. Interestingly these observations are in agreement with earlier observations [40] but are contrary to reports for coordination compounds of copper(II) chloride and bromide with cyanoanniline wherein bonding through $–NH_2$ has been reported [41]. The absorption band due to ν(CN) mode occurring at 2242 cm^{-1} has been observed to shift higher wave number by 25-30 cm^{-1} indicative of coordination through nitrile group (Fig. 5a)

The υ(C≡N) mode, known to occur at 2240 cm^{-1} in 2-cyanopyridine has been observed to remains almost unaltered, suggesting thereby the non-participation of cyano group in coordination. The coordination through the pyridine ring nitrogen is known to lead to characteristic blue shifts in the positions of pyridine ring vibrations viz. four principal

bands of pyridine in 1600-1430 cm^{-1} region due to C=C and C=N stretching vibrations move to higher wave number on coordination, with the highest frequency band giving the largest shift without much change in the position of υ(CN). Bonding through pyridine nitrogen is further supported by the appearance of bands in 338-325 cm^{-1} region assigned to υ(V←N) mode establishing hereby that the coordination of cyanopyridine has occurred through ring nitrogen (Fig. 5b).

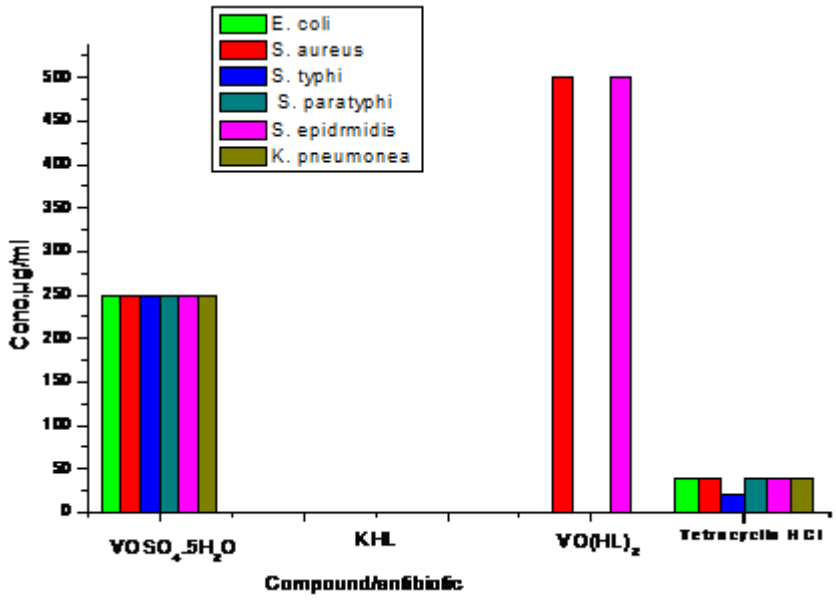


(a) **(b)**

Fig. 5 Geometry of addition compound of bis(nicotinohydroxamato)oxidovanadium(IV) complex

Antibacterial activity

The $VOSO_4.5H_2O$, ligands and newly synthesized complex was tested *in vitro* for their antibacterial activity against Gram +ve bacteria viz. *Staphylococcus aureus, Staphylococcus epidermidis and Gram –ve bacteria Escherichia coli, Salmonella typhi, Salmonella paratyphi and Klebsiella pneumoniae* employing MIC method [graphic 1]. The results were compared with treated control, commercial antibiotic tetracycline hydrochloride which inhibited bacteria in 7.81-15.62 µg/mL range. The results show that the $VOSO_4.5H_2O$ inhibits all the bacteria at 250 µg/mL. The ligand has been found to show no effect on different bacterial strain under consideration. The complex do not exhibit any significant activity for any of tested bacteria (table 4).



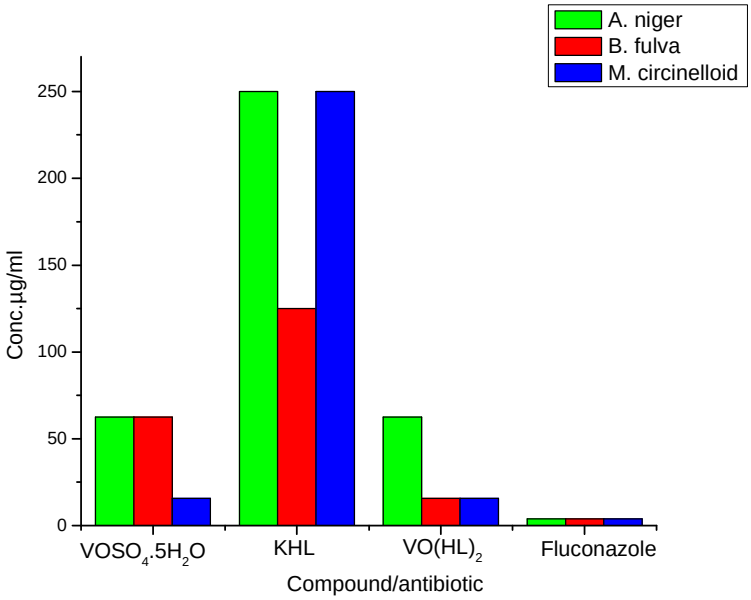
Graphic 1: In vitro antibacterial spectrum of bis(nicotinohydroxamato)oxidovanadium(IV) complex

Table 4: Antibacterial data of bis(hydroxamato)oxidovanadium(IV) Complex

Ligand/Complex	Bacteria					
	E.coli	*S.aureus*	*S.typhi*	*S.paratyphi*	*S.epidermidis*	*K.pneumonea*
$VOSO_4.5H_2O$	250	250	250	250	250	250
KHL	-	-	-	-	-	-
$VO(HL)_2$	-	500	-	-	500	-
Standard drug tetracycline hydrochloride	15.62	15.62	7.81	15.62	15.62	15.62

Antifungal activity

The $VOSO_4.5H_2O$, KHL and $VO(C_5H_4NCONHO)_2$ were screened in vitro for their antifungal activity on selected fungi *A. niger, B. fulva* and *M. circenelloids* using MIC method (table 5). The results were compared with standard antifungal drug fluconazole (treated control) which inhibits these fungi at 3.9 µg/mL. The $VOSO_4.5H_2O$ inhibits the growth of selected fungi *A. niger and B. fulva* at 62.5 µg /mL and *M. circenelloids* at 15.62 µg /mL. The ligand inhibits fungi *A. niger M. circenelloides* at 250 µg /mL *and B. fulva* at 125 µg /mL.



Graphic 2: In vitro antifungal spectrum of bis(nicotinohydroxamato)oxidovanadium(IV) complex

Complex has shown pronounced activity at 15.62 µg/mL against *B. fulva* and *M. circinelloides and A. niger* at 62.5 µg/mL. Although the antifungal activity of complexes is less than standard fungicide yet is relatively higher than earlier reported monooxidovanadium(IV) complex (graphic 2). Further it has been reported that complex $VO(HL^2)_2$ show significant antifungal activity, although antibacterial activity of this complex is negligible.

Table 5: Antifungal data of bis(nicotinohydroxamato)oxidovanadium(IV) Complex

Ligand/Complex	Fungi		
	A. niger	B.fulva	M. circinelloid
$VOSO_4.5H_2O$	62.5	62.5	15.62
KHL	250	125	250
$[VO(HL)_2]$	62.5	15.62	15.62
Standard drug (fluconazole)	3.9	3.9	3.9

In Vitro Cytotoxicity Assay. Cytotoxic assays of $VOSO_4$, potassium nicotinohydroxamate and newly synthesized complex was performed at several concentrations by means of colorimetric microculture MTT assay (table 6). Complex exhibit appreciable viability of 83.5% respectively at 2mM concentration. It has been observed that with increase in concentration of test complex cytotoxicity gets significantly enhanced. The cytotoxic study has shown that complex derived from nicotinohydroxamate are less toxic.

Table 6. Cytotoxic assay of hydroxamate ligand and bis(nicotinohydroxamato)oxidovanadium(IV) complex against Hep2C cell line

Test Compound	Cell viability (%) at the selected test compound concentration					
	Control	2mM	4mM	8mM	20mM	28mM
$VOSO_4.5H_2O$	100	40	35	35	30	30
$C_5H_4NCONHOK$	100	44.8	44.8	42.1	38.9	39.3
$VO(C_5H_4NCONHO)_2$	100	83.5	83.0	83.0	48.8	48.8

CONCLUSION

The hydroxamato oxidovanadium(IV) complex derived from nicotinohydroxamate ligand has been synthesized and thoroughly characterized by various physicochemical and spectral techniques and a square pyramidal geometry around vanadium in these coordination compounds has been inferred. IR spectral studies show the bidentate nature of hydroxamate ligands involving coordination through hydroxylamine oxygen (-NHO) and carbonyl oxygen

(C=O). A square pyramidal geometry around vanadium is consistent with various spectroscopic studies. The electrochemical studies have shown these to exhibit quasi-reversible V^{V}/V^{IV} redox couple. The complexes have shown promising biological activity against tested pathogenic bacteria and fungi. The coordination compounds of parent complexes with nitrogenous bases 2-cyanopyridine and 4-aminobenzonitrile have been prepared and characterized in order to study the bonding behavior of bases.

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