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Synthesis, characterization, electrochemistry and antimicrobial activities of bis(hydroxamato)oxidovanadium (IV) complexes

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ABSTRACT

The bis (hydroxamato)oxidovanadium(IV) complexes of composition $[VO(HL^{1,2})_2]$ { $[HL^1$ = 4-$NO_2C_6H_4$ CONHO]$^-$, 4-nitrobenzohydroxamate; HL^2 = $[2\text{-Cl-4-}NO_2C_6H_3CONHO]^-$ 2-chloro-4-nitrobenzohydroxamate} have been synthesized by the reactions of $VOSO_4.5H_2O$ with two equivalents of potassium salts of respective hydroxamic acids in aqueous methanol. The characterization of complexes has been accomplished by elemental analyses, molar conductivity, magnetic moment measurements, electronic and spectral (IR, ESR and mass) studies. The magnetic moment and ESR spectra indicated +4 oxidation state of vanadium. The IR spectra suggested bonding through hydroxylamine and carbonyl oxygen (O,O coordination). Inferred from spectral studies a square-pyramidal geometry around vanadium has tentatively been proposed for complexes. The thermal behavior of complexes has been studied by TGA technique. The antimicrobial activities of the newly synthesized complexes, ligands and precursor have been evaluated against some pathogenic bacteria E.coli, S.aureus, S.typhi, S.paratyphi, S.epidermidis and K.pneumoniae and fungi A. niger, B. fulva and M. circinelloides by minimum inhibitory concentration method. The complexes exhibited promising antimicrobial activity relative to free ligands and standard drug compounds. The coordination compounds of complexes with 2-cyanopyridine and 4-aminobenzonitrile have also been synthesized and characterized by physicochemical and IR spectral technique.

Keywords: Bis(hydroxamato)oxidovanadium(IV) complexes, Potasium-4-nitrobenzohydroxamate and 2-chloro-4-nitrobenzohydroxamate, Antimicrobial activity

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INTRODUCTION

Over the years, the coordination chemistry of vanadium has drawn enormous research interest owing to the potential applications of vanadium complexes in catalysis [1-5] therapeutics [6-14], material science [15-16] and magneto-structural study of polynuclear species [17]. The biological relevance of vanadium regarding the essentiality, distribution and toxicity in +4 and +5 oxidation state has been abundantly established. The vanadate and some peroxovanadate complexes have been reported to exhibit insulin enhancing potency [18-20]. VO^{2+} is known to possess extensive clinical applications [21-22]

Of numerous ligands known to form metal complexes, the hydroxamic acids RCONHOH have been proved to be excellent ligands with -NHOH moiety as constituent of antibiotics [23], growth factors, [24] food additives, tumor inhibitors and cell division factors. Owing to the pharmacological [25-26] toxicological [27] and pathological properties [28-29] of hydroxamic acids, their biological [30] and medicinal applications [31] are well- documented [32]. The strong ability of hydroxamic acids to form chelates is related to their biological effects. The hydroxamic acids display a range of coordination sites depending on metal ion involved [33] and pH of the reaction solution [34]. Hydroxamic acids, R-CONHOH, are inhibitors specific to the respiratory pathway wherein the nature of R group in compounds affects the concentration at which the hydroxamic acids are effective. Literature contains reports that some –nitro and –chloroheterocycles exhibit diverse biological activity viz. anti inflammatory,

vasodilator activity and structure activity relationship have been used in sedatives, hypnotics and antimicrobials [35-36]. The chlorohydroxamic acid have been found to be the most effective antitumor agent [37]. The 2-nitro-5-(sulphophenoxy) hydroxamic acid derivatives are known to possess herbicidal activity. Further it has been reported that nitro heterocycles have good antifungal activity rather than antibacterial activity.

In view of the biological relevance of vanadium metal, hydroxamate ligands and as part of our ongoing investigations on the synthesis of vanadium hydroxamate complexes [38-41] the present manuscript describes the synthesis of oxidovanadium(IV) complexes, derived from 4-nitrobenzohydroxamate and 2-Chloro-4-nitrobenzohydroxamate ligands since a few scattered reports are met in literature on nitro- substituted hydroxamic acids [42-44]. The newly synthesized complexes have been thoroughly characterized and evaluated for their antimicrobial activity.

MATERIALS AND METHODS

All the solvents used were of A.R. grade and were dried by standard methods. Vanadyl sulphate ($VOSO_4.5H_2O$) (Merck) was used as procured. The potassium 4-nitrobenzohydroxamate and potassium 2-chloro-4-nitrobenzohydroxamate were synthesized by reported method [45] and characterized by IR spectra. The vanadium content in complexes was determined gravimetrically as V_2O_5. The elemental analyses were performed on Carlo-Erba 1108 elemental Analyzer. The conductivity measurements in nitrobenzene were made on an Elico conductivity bridge type CM-82T. The room temperature magnetic susceptibilities were measured by Gouy's method using $Hg[Co(NCS)_4]$ as calibrant. FTIR spectra of complexes were collected on a Nicolet-5700 FTIR spectrophotometer (4000-200 cm^{-1}) using KBr pellets. Electronic spectra of complexes were recorded on a Varian Cary-100 Bio UV-Vis. spectrophotometer using methanol as solvent. The mass spectrum were recorded at room temperature as electron spin ES^+ mass spectra. Thermograms of complexes were recorded in nitrogen atmosphere at a heating rate of 20 ^0C min^{-1}.

2.2 Synthesis of $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I) and $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2$ (II) :

In a typical reaction to a solution of potassium 4-nitrobenzohydroxamate (1g, 0.0045mol) and potassium 2-chloro-4-nitrobenzohydroxamate (1g, 0.0039 mol) in methanol (20mL) was added vanadyl sulphate (0.57g, 0.0022 mol, 0.49g, 0.0019 mol respectively) dissolved in minimum quantity of distilled water (5mL) in separate experiments. The reaction mixture was stirred for 8 h when initial blue color of reaction mixture changed to dark brown and separation of solid was observed. It was then filtered and was washed with methanol and petroleum ether. The complexes were recrystallized from dichloromethane. Yield: $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I) 0.9g, (88%); $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2$ (II) 0.85g, (87%). Anal. Calcd. for $C_{14}H_{10}N_4O_9V$ $[VO(4\text{-}NO_2C_6H_4CONHO)_2]$ (Formula weight, 429) (%): C, 39.16; H, 2.33; N, 13.05, V, 11.88. Found: C, 39.22; H, 2.39; N, 13.11; V, 11.56; Λ_m =1.27 Scm^2mol^{-1}; μ_{eff} ; 1.72 B.M. Anal. Calcd. for $C_{14}H_8N_4O_9VCl$ $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2]$ (Formula Weight, 498) (%) C, 33.74; H, 1.60; N, 11.24; V, 10.23. Found: C, 33.82; H, 1.55; N, 11.29; V, 10.15; Λ_m = 2.43 Scm^2mol^{-1}; μ_{eff}; 1.74 B.M. .

2.3 Preparation of Coordination compounds of $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I) and $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2$ (II) with 2-cynopyridine and 4-aminobenzonitrile:

To a methanol solution of $[VO(4\text{-}NO_2C_6H_4CONHO)_2]$ $(VO(HL^1)_2)$ and $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2]$, $(VO(HL^2)_2)$ 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 dark color solid was observed. The solid compounds so obtained were treated petroleum ether and finally dried under vacuum. Anal. Calcd. for $[VO(4\text{-}NO_2C_6H_4CONHO)_2.2\text{-}Cyanopyridine]$; $C_{20}H_{14}N_6O_9V$, (Formula weight, 533) (%): C, 45.02; H, 2.62; N, 15.75; V, 9.56. Found: C, 45.10; H, 2.70; N, 15.78; V, 9.60 Λ_m =1.80 Scm^2mol^{-1}; μ_{eff} ; 1.73 B.M.. Anal. Calcd. For $VO(4\text{-}NO_2C_6H_4CONHO)_2.4\text{-}aminobebenzonitrile]$ $C_{23}H_{15}O_5N_6V$, (Formula weight, 546) (%): C, 50.54; H, 2.74; N, 15.38; V, 9.34. Found: C, 50.60; H, 2.80; N, 15.40; V, 9.40; Λ_m =2.09 Scm^2mol^{-1}; μ_{eff} ; 1.74 B.M.. Anal. Calcd. for $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2.2\text{-}cyanopyridine]$ $C_{20}H_{14}N_6O_9V$, (Formula weight, 602) (%) : C, 39.86; H, 2.32; N, 13.95; V, 8.47. Found: C, 39.88; H, 2.38; N, 13.99; V, 8.50 Λ_m =4.79 Scm^2mol^{-1}; μ_{eff} ; 1.76 B.M.. Anal. Calcd. for $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2.4\text{-}aminobenzonitrile]$ $C_{21}H_{16}N_6O_9V$ (Formula weight, 615) (%): C, 40.97; H, 2.60; N, 13.65; V, 8.29. Found: C, 40.99; H, 2.64; N, 13.68; V, 8.34; Λ_m = 4.50 Scm^2mol^{-1}; μ_{eff} ; 1.70 B.M..

2.4 Antimicrobial activity test

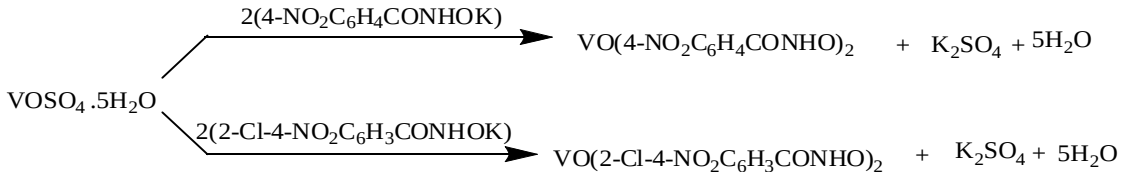
2.4.1 MIC determination by two-fold serial dilution

The *in vitro* antibacterial and antifungal activity of oxidovanadium(IV) complexes were studied against fungi and Gram (+ve) and Gram (-ve) bacteria by a minimum inhibitory concentration (MIC) method [46]. MIC is the lowest concentration of the antimicrobial agent that prevents visible growth after overnight incubation. All the samples were tested in triplicate. All 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 complex 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 complex. 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}). The broth in each well was inoculated with 2µL of the bacterial culture and the contents were mixed by ten clockwise and ten anticlockwise rotations on flat surface. The plate was incubated at 35^0C and observations for growth of bacteria were recorded after 24h.

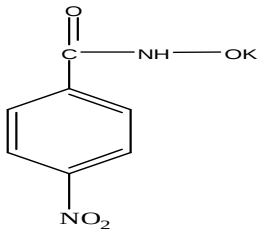
RESULTS AND DISCUSSION

The reaction of $VOSO_4.5H_2O$ with two equivalents of potassium 4-nitrobenzohydroxamate and 2-chloro-4-nitrobenzohydroxamate viz. KHL^1, KHL^2 (Fig.1) afforded the quantitative formation of complexes in confirmation with elemental analysis according to the following equations:

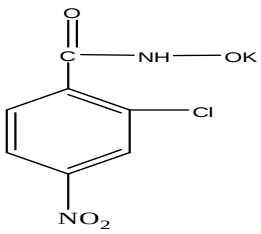


Scheme 1. Syntheses of bis(hydroxamato) oxidovanadium(IV) complexes

The complexes are dark brown in color and are insoluble in most of organic solvents but soluble in methanol and dimethylsulphoxide. The elemental analysis data agree well with the proposed formulae for ligands and also confirmed $VO(HL^{1,2})_2$ composition of the complexes. Efforts to grow good crystal of the ligands and their metal chelates for X-ray diffraction studies were unsuccessful due to their poor solubility in common organic solvents. The molar conductance value of millimolar solution of the complexes in nitrobenzene (1.27 and 2.43 Scm^2mol^{-1}) indicating their non electrolytic nature and solubility problem. The room temperature magnetic moment values of the complexes (I) and (II) are 1.72 and 1.74 B.M. respectively consistent with +4 oxidation state of vanadium.



KHL^1



KHL^2

Fig. 1

3.1 IR Spectra

The formation of complexes was ascertained from a comparison of IR spectra with that of free hydroxamate ligands 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. The absorption bands due to υ(C=O) mode in metal free 4-nitrobenzohydroxamate and 2-Chloro-4-nitrobenzohydroxamate ligands have been observed in 1620 and 1589 cm^{-1} region. The newly synthesized oxidovanadium (IV) complexes have displayed band due to υ(C=O) mode at 1586 cm^{-1}, 1550 cm^{-1}, in respective complexes. The shift of υ(C=O) mode to lower frequency is indicative of bonding through carbonyl oxygen. The absorption band due to υ(C–N) mode occurring at 1376 and 1344 cm^{-1} in respective free ligands appeared at 1382 and 1385 cm^{-1} in complexes. The sharp bands occurring at 935 cm^{-1}, 945 cm^{-1} in KHL^1, KHL^2 respectively ascribed to υ(N–O) mode have appeared at 948 -920 cm^{-1} in respective complexes, indicative of bonding through hydroxylamine oxygen [47]. The absorption bands occurring at 3230 cm^{-1} and 3222 cm^{-1} assigned to υ(N–H) in KHL^1 and KHL^2 remains nearly unaltered which excludes the possibility of bonding through nitrogen. The characteristic bands due to υ (V=O) mode appeared at 984 and 980 cm^{-1} in $[VO(4\text{-}NO_2C_6H_4CONHO)_2]$ and $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2]$ respectively are suggestive of square-pyramidal geometry around vanadium. The bands occurring in 575-534 cm^{-1} region have been assigned to υ(V-O) mode in complexes. The non-observance of bands at 785 cm^{-1} assignable to V-O-V asymmetric stretch are indicative of mononuclear nature of complexes. The absorption bands observed in 1590-1520 cm^{-1} have been ascribed to υ (NO_2) mode.

3.2 Magnetic studies

The room temperature magnetic moment of 1.70 and 1.75 B.M. for complexes $[VO(4\text{-}NO_2C_6H_4CONHO)_2]$ and $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_4CONHO)_2]$ respectively, in accordance with value expected for d^1, S=1/2 systems, establish the existence of mononuclear and paramagnetic nature of complexes.

3.3 Electronic Spectra

The UV-Vis spectra of vanadium precursor, ligands and newly synthesized complexes have been recorded in methanol. The electronic absorption spectra of $VOSO_4.5H_2O$ exhibited bands at 252, 306 and 780 nm a peculiar feature of vanadyl complexes [48]. The ligands KHL^1 and KHL^2 showed bands at 255, 364, 398, 416 nm and 288, 362, 386, 400 nm respectively attributed to intraligand $\pi\rightarrow\pi^*$ transitions.

The complexes $[VO(4\text{-}NO_2C_6H_4CONHO)_2]$ and $[VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_4CONHO)_2]$ displayed bands at 364, 396, 500, 690 nm and 288, 352, 540, 698 nm respectively. Electronic absorption bands in 540-400 nm region are ascribed to LMCT transition. These spectral observations are in agreement with those reported for square- pyramidal oxidovanadium(IV) complexes.

3.4 ESR Spectra

The room temperature X-band ESR spectra of bis(hydroxamato)oxidovanadium(IV) complexes exhibited eight well resolved lines due to the interaction of an unpaired electron of vanadium(IV) center with its own nucleus, I= 7/2 in accordance with a single paramagnetic species of vanadium(IV). The g_{av} values determined from spectra are ≈1.98 similar to spin only value (free electron value of 2.00) suggesting little spin orbital coupling.

3.5 Mass Spectra

The major ES^+ MS peaks observed for oxidovanadium(IV) hydroxamate complexes are given. The complexes $[VO(HL^1)_2]$ (I) and $[VO(HL^2)_2]$ (II) exhibited low intense molecular ion peak at m/z (%) 429(3.75) and 498(4.98) respectively. The base peak at m/z 453 (75) and 255(100) in complexes (I) and (II) corresponded to $[VO(HL^1)_2 +Na+H]^+$ and $[VO(HL^2) -CO]^+$ respectively. The other structurally important intense peaks in (I) occurring at m/z $[HL^1\text{-}NHO+H]^+$; 150(36.76), HL^1; 182(17.96), $[VO(HL^1)_2\text{-}HL^1\text{-}NO_2+3H]^+$; 205(40.90), $[VO(HL^1)_2\text{-}2NO_2+H^+]$;338 (56.99) respectively.

The absence of peaks at higher m/z value than molecular mass are indicative of monomeric nature of complexes. Complex of composition $[VO(HL^2)_2$ exhibited peaks at $[VO(HL^2)_2\text{-}CO+2H]^+$; 472(4.92), $[HL^2\text{-}NHO\text{-}H]^+$; 186(5.63), $[VO(HL^2)_2\text{-}HL^2\text{-}NO_2+3H]^+$; 239(18.06), $[HL^2\text{-}Cl+3H]^+$ 184(5.63), $[VO(HL^2)_2\text{-}2H^+]$;496(5.27) respectively. Based upon physicochemical and FTIR, UV-Vis. and mass spectral data coupled with magnetic moment measurements, square pyramidal geometry around vanadium may tentatively be proposed (Fig. 2,3).

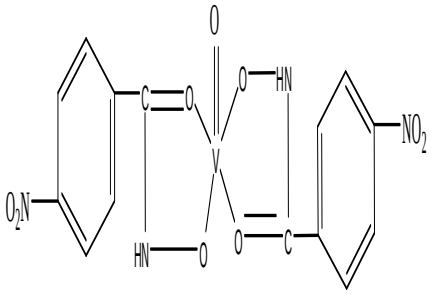


Fig.2

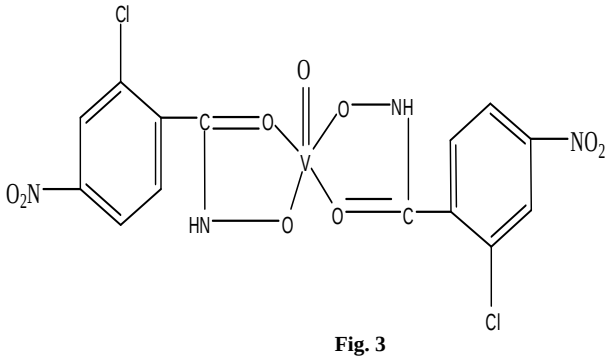


Fig. 3

Table: 1 Mass Spectral table of Bis(hydroxamato)oxidovanadium(IV) Complexes

Complex	m/z(%)	Complex	m/z(%)
$[VO(HL^1)_2]$	429(3.75)	$[VO(HL^2)_2]$	498(4.98)
$[VO(HL^1)_2+Na+H]^+$	453(75)		
$[VO(HL^1)_2\text{-}O]^+$	413(6.46)	$[VO(HL^2)_2\text{-}2\ H]^+$	496(5.27)
		$[VO(HL^2)_2\text{-}CO+2\ H]^+$	472(4.92)
		$[VO(HL^2)_2\text{-}Cl\text{-}NO_2\text{-}3H]^+$	413(4.44)
$[VO(HL^1)_2\text{-}NO_2+6H]^+$	389(4.51)	$[VO(HL^2)_2\text{-}2Cl\text{-}2NO_2\text{-}4H]^+$	332(3.08)
$[VO(HL^1)_2\text{-}2NO_2+5\ H]^+$	338(56.99)	$[VO(HL^2)_2\text{-}HL^2\text{-}NO_2+3H]^+$	239(18.06)
$[V(HL^1)_2\text{-}HL^1\text{-}5H]^+$	244(28.94)	$[VO(HL^2)\text{-}CO]^+$	255(100)
$[VO(HL^1)_2\text{-}HL^1\text{-}NO_2+3H]^+$	205(40.90)	$[HL^2+CO\text{-}2H]^+$	242(3.06)
$[HL^1]$	182(17.96)	$[HL^2]^+$	216(7.72)
$[HL^1\text{-}NHO+H^+]$	150(36.76)		
		$[HL^2\text{-}Cl+3H]^+$	184(5.63)

3.6 Cyclic Voltammetery

Cyclic Voltammetery is a versatile electrochemical technique which allows to probe the mechanics of redox and transport properties of a system in solution or microcrystalline solid state. Its versatility combined with the ease of measurement has resulted in extensive use in fields of redox electrochemistry of coordination compounds, organic chemistry and biochemistry. This technique yields information about reaction reversibility and also offers a very rapid means of analysis for suitable system. The method is not only valuable for the investigation of stepwise reactions but also for direct investigation of reactive intermediate. The systems exhibiting a wide range of rate constants and transient species with half lives of the order of milliseconds can be studied by varying the scan rate. The voltammetric data of complexes is taken as a criterion of complex stability.

Table 2: Cyclic voltammetric Data for bis(hydroxamato)oxidovanadium(IV) Complexes

Complex	Scan rate mV/sc	Redox couple	Epa (V)	Epc (V)	ΔE (mV)
$[VO(HL^1)_2]$	100	VO^{3+}/VO^{2+}	-0.5653	-0.4542	-11.11
$[VO(HL^1)_2]$	150	VO^{3+}/VO^{2+}	-0.4610	-0.6165	15.55
$[VO(HL^1)_2]$	200	VO^{3+}/VO^{2+}	-0.6208	-0.3431	-27.77
$[VO(HL^2)_2]$	100	VO^{3+}/VO^{2+}	-0.6763	-0.7141	3.78
$[VO(HL^2)_2]$	200	VO^{3+}/VO^{2+}	-0.5098	-0.7518	15.38

Owing to the variable oxidation states exhibited by vanadium, the reduction/oxidation is known to occur between different oxidation states without the involvement of ligand molecule [49]. The one electron reactions for vanadium complexes are represented as:

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

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

$$V^{IV}O \rightleftharpoons V^{V}O - e^{-1} \quad (3)$$

In order to probe the electrochemical properties of oxidovanadium(IV) hydroxamate complexes $[VO(HL^1)_2]$ (I) and $[VO(HL^2)_2]$ (II) the cyclic voltammetric measurements in MeOH/H_2O (5:95) at different scan rates 100mV s^{-1}, 150 mV s^{-1} and 200 mV s^{-1} have been performed. The initial scan in the anodic direction in -2.0 v to +2.0 v range of complexes displayed single prominent cathodic and anodic peak at negative potentials suggesting thereby that oxidovanadium(IV) compounds can be oxidized at distinctly lower potential. The peak potentials have been found to correspond to one electron change and no reversible reductions have been found for the complexes under study [50]. The separations between cathodic and anodic peak are indicative of quasi-reversible behavior [51-52] of V^V/V^{IV} redox couple. The negative potentials of V^V/V^{IV} couple in the complexes are indicative of their stability suggesting thereby that oxidovanadium(IV) complexes can be oxidized at distinctly lower potential. The electrode process can therefore be represented as:

$$[VO^{IV}(HL)]^0 \rightleftharpoons [VO^{V}(HL)]^+ \quad (4)$$

The variation of the scan rate between 100 mV s^{-1} and 200 mV s^{-1} showed marginal to appreciable increase in peak potential (ΔE_p) (Table. 4) indicating thereby that the reaction is quite slow and of are quasi-irreversible nature.

3.7 Thermal Studies

The thermal decomposition behavior of complexes $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I) and $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_4CONHO)_2$ (II) has been studied by TGA technique in N_2 atmosphere (Table 3). The TG curves of complexes (I) and (II) (Figs. 4 and 5) have shown these to be thermally stable up to 30.11 ^{0}C and 24.80 ^{0}C, respectively, after which temperature the complexes (I), (II) have been observed to undergo two and three step decomposition respectively.

In case of $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I), the initial mass loss of 20.19% in 30.11-151.87^{0}C temperature range accounted for the loss of two -NO_2 groups. The mass loss of 28.2% in second step corresponded to the loss of one ligand HL^1 yielding black-colored residue VO_2 with some contaminated organic matter.

Complex of composition $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_4CONHO)_2$ (II) showed an initial mass loss of 10.59% in temperature range 24.80-130.75 ^{0}C accounting for the loss of –NO_2 group from one ligand. The mass loss of

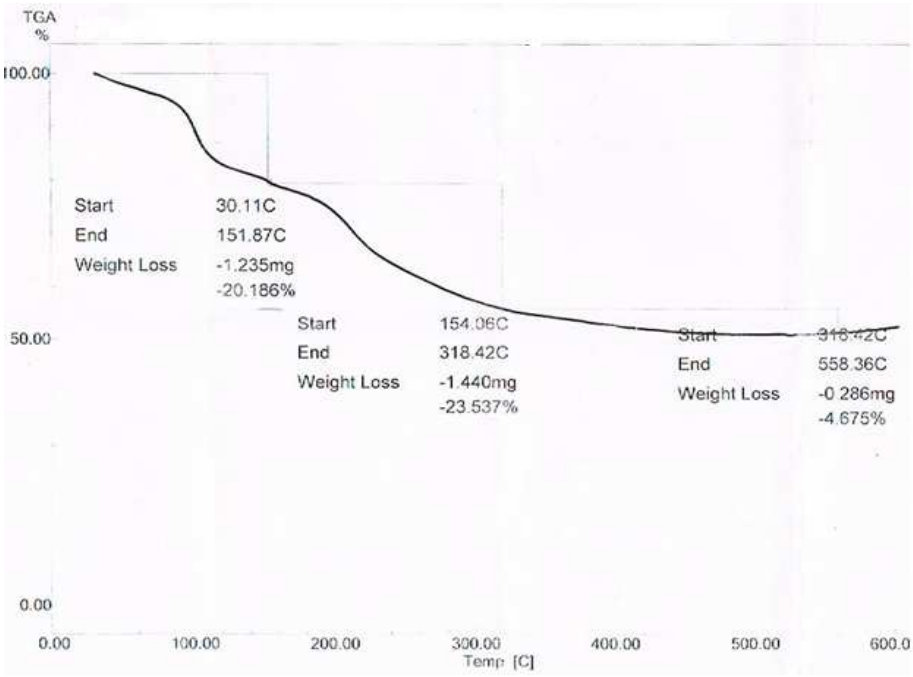


Fig.4

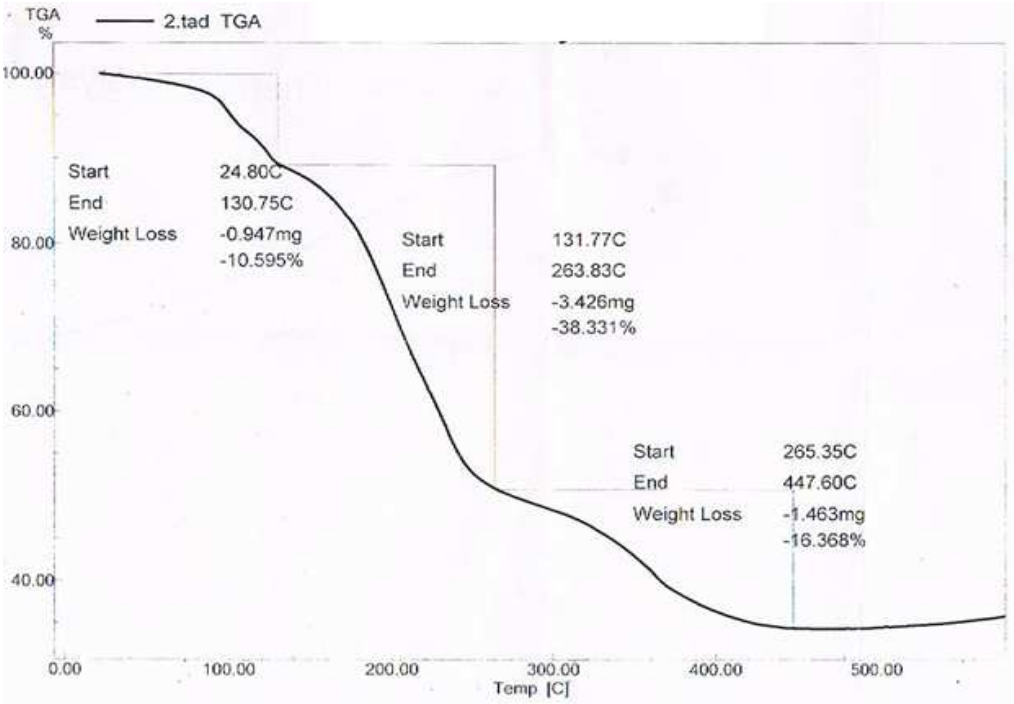
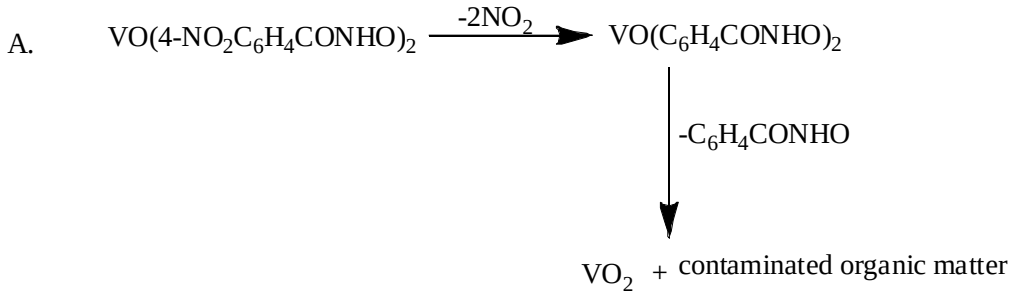
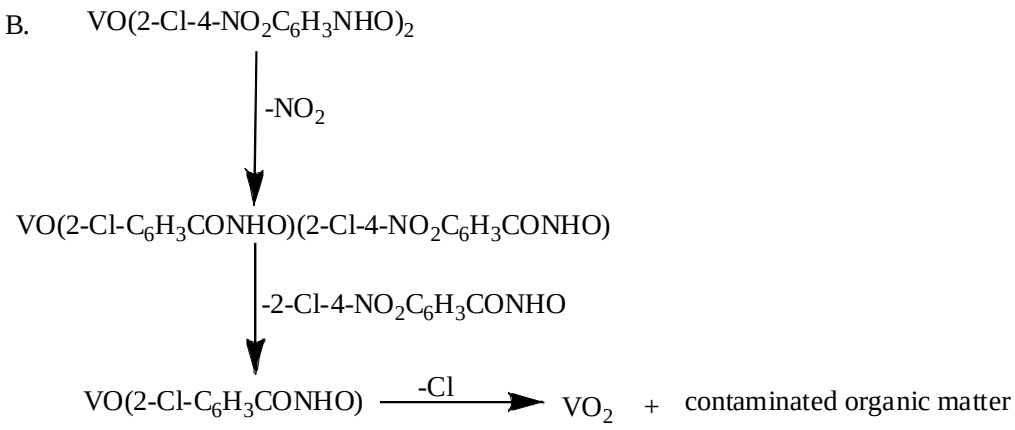


Fig. 5

38.31 % in temp. range of 131.77 - 447.60 ^{0}C in second stage of decomposition corresponded to the loss of HL^2 group. The mass loss of 16.38% in third step corresponded to the loss of –Cl group yielding VO_2. Compared to the formation of V_2O_5 as the final product of decomposition in most of the vanadium complexes, the formation of VO_2 in complexes under study is in agreement with our earlier observations [53-54]. The formation of VO_2 as thermolysed product of oxidovanadium(IV) hydroxamate complexes has been confirmed by IR spectra of residue. The IR spectra of residue showed characteristic absorption bands of VO_2 occuring due to υ (V=O) and υ (V-O) mode at 990 cm^{-1} and 670, 652, 615, 525 and 325 cm^{-1} respectively [55-56].



Scheme2. Thermal decomposition scheme of $VO(HL^1)_2$



Scheme 3. Thermal decomposition scheme of $VO(HL^2)_2$

Table 3: Thermal decomposition data of bis(hydroxamato)oxidovanadium(IV) Complexes

Complex	Initial decomposition temperature (^{0}C)	Stages of decomposition (^{0}C)	TGA Data		
			Decomposition Range	Weight loss (%)	Decomposition Products
$VO(HL^1)_2$	30.11	1st	30.11-151.87	20.19	$VO(HL^1)_2$ -$2NO_2$
		2nd	151.87-558.36	28.2	$VO(HL^1)_2$ - HL^1- NO_2
$VO(HL^2)_2$	24.80	1st	24.80-130.75	10.59	$VO(HL^2)_2$- NO_2
		2nd	131.77-263.83	38.31	$VO(HL^2)_2$-NO_2- HL^2
		3rd	265.35-447.60	16.38	$VO(HL^2)_2$-NO_2- HL^2-Cl-O

On the basis of analytical and IR, UV-Vis. and mass spectral data a distorted square pyramidal geometry for oxidovanadium(IV) hydroxamate complexes has been proposed and representative structures for the complexes are given (Figs. 5,6).

3.8 Coordination compounds of $[VO(HL^{1,2})_2]$ with 2-cynopyridine and 4-aminobenzonitrile:

The 2-cyanopyridine and 4-aminobenzonitrile are known to possess extensive coordination chemistry and display interesting coordination behavior owing to the presence of two potential donor sites viz. pyridine nitrogen and the nitrile nitrogen in former and nitrile nitrogen, nitrogen of amino group in case of 4-aminobenzonitrile. Information for the formation of these adducts and bonding modes of nitrogenous bases has been ascertained from comparison of IR spectra of isolated coordination compounds with that of free bases. The diagnostic coordination sensitive bands of cyanopyridine are nitrile stretching υ(CN), υ(C=C) and υ(C=N) ring stretching and ring breathing frequencies. The υ(C≡N) mode, known to occur at 2240 cm^{-1} in 2-cyanopyridine has been observed at 2235 cm^{-1} and 2238 cm^{-1}, remains almost unaltered which may be attributed to both resonance and electronic effects from π–back bonding with metal, suggesting thereby the non-participation of cyano group in coordination. The bands occurring in 1600-1400 cm^{-1} and 1080-965 cm^{-1} regions have however been found to move towards higher wave numbers suggesting the coordination of these bases through pyridine ring nitrogen only. 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). The ring breathing frequencies and C–H inplane deformations occurring in the 1250-985 cm^{-1} region have been also been found to shift to higher wave number. Bonding through pyridine nitrogen is further supported by the

appearance of bands in 338-325 cm^{-1} region assigned to υ(V←N) mode [57] establishing thereby that the coordination of cyanopyridine has occurred through ring nitrogen.

The principal bands of cyanoannilines which are expected to undergo significant changes are due to υ(CN) mode occurring at ~ 2240 cm^{-1} and υ (NH) asymmetric and υ (NH) symmetric modes appearing around ~ 3440 cm^{-1} and ~ 3360 cm^{-1} in uncoordinated cyanoanilines. It is generally interpreted that a decrease in υ(CN) mode is results from coordination of cyano group through its triple bond while coordination through – NH_2 group leads to characteristic negative shift. The IR spectra of coordination compounds of 4-cyanoanilines have shown that bands due to υ_{asym} (NH) and υ_{sym} (NH) mode have remained almost unaltered upon coordination. A significant shift by 30-40 cm^{-1} in υ(CN) mode towards higher wave number has been observed in coordination compounds. These observation suggest that nitrogen of amino (-NH_2) group is not involved in coordination to the metal while nitrile (CN) gets coordinated to the metal through its nitrogen. Sharp and distinct bands observed around ~320 cm^{-1} in the coordination compounds have been assigned to υ(V←N) modes. An explanation for the observations in the coordination compounds oxidovanadium(IV) hydroxamates with 4-cyanoanniline have shown that nitrogen of nitrile group and not amino group may be given in terms of inherent electron withdrawing property of nitrile group from the ring through resonance which thereby reduces the donor character of amino group in cyanoaniline. The absence of bands due to υ (V=O) occurring at 935 and 978 cm^{-1} in present complexes was found to shift to lower frequency in 930-910 cm^{-1} region in addition compounds [56]. This observed bands may be attributed to the electronic donation of the base to vanadium (N→V), which increases the electron density on the metal d-orbitals, and consequently the $p_\pi \rightarrow d_\pi$ donation from the oxygen atom to vanadium is expected to be reduced. On the basis of above data, a six-coordinate distorted octahedral geometry around vanadium (Figs. 5, 6, 7, 8) may tentatively be proposed for coordination compounds.

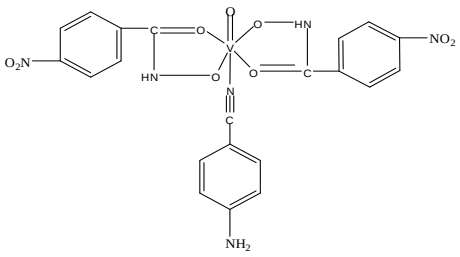


Fig. 5

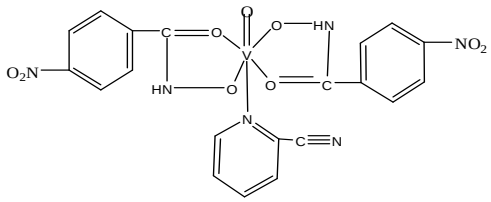


Fig. 6

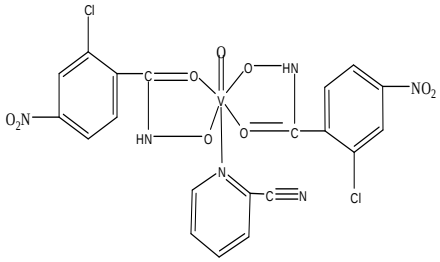


Fig. 7

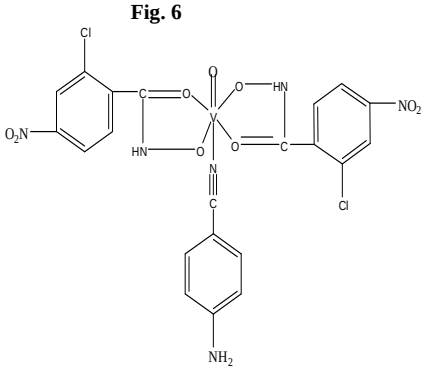


Fig. 8

3.9 Antibacterial activity

The vanadium precursor, ligands and newly synthesized complexes were 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. The results were compared with treated control, commercial antibiotic tetracycline hydrochloride which inhibited bacteria under study in 7.81-15.62 µg/mL range. The results show that the $VOSO_4.5H_2O$ inhibits all the bacteria at 250µg/mL. The KHL^1 inhibits *S. epidermidis, E. coli, S. paratyphi and K. pneumoniae* at 250 µg/mL and for *S. aureus, and S. typhi* at 125 µg/mL. The KHL^2 has been found to inhibit *S. typhi* at 3.9 µg/mL and *S. aureus at* 62.5 µg/mL , while remaining other bacteria are inhibited at 125 µg/mL.

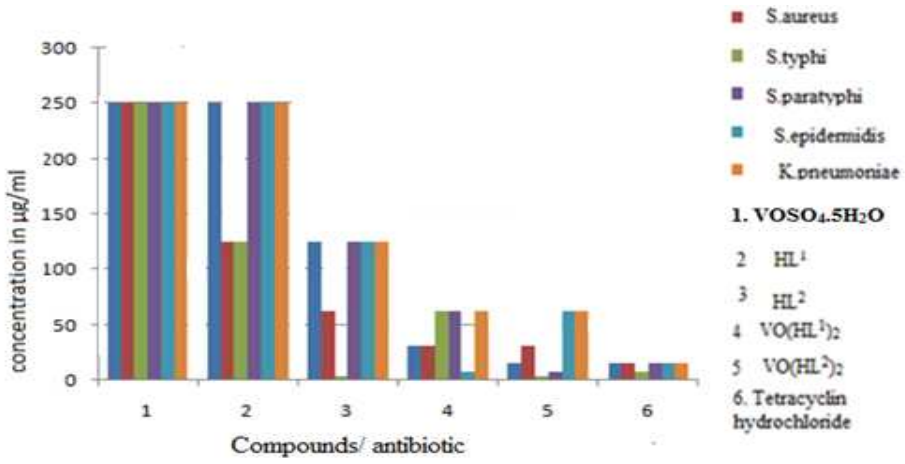
Complex $[VO(HL^1)_2]$ has shown remarkable inhibitory effect against *S. epidermidis* at 7.81 µg/mL and against *S. aureus and E. coli* at 31.25 µg/mL. Complex $VO(HL^2)_2$ has shown significantly enhanced inhibitory activity. The complex $VO(HL^2)_2$ has shown enhanced activity against *S. paratyphi* at 7.81 µg/mL (Table 4) relative to free ligand

but similar to ligand against *S. typhi*. The activity have been observed to increase considerably on complexation. An explanation to the observed promising antibacterial activity of complexes can be attributed to the biological significance associated with vanadium, hydroxamate ligands and efficient diffusion due to reduction of the polarity of central metal ion because of partial sharing of its positive charge with the ligand on coordination which favors permeation of the complexes through the lipid bilayer of cell membrane [58]. The antibacterial activity of –Cl substituted hydroxamate ligand as well as complex has been reported to be more than the $–NO_2$ substituted hydroxamate ligand and respective complex, probably due to +I effect of –Cl gp. This in turn is responsible for increasing the hydrophobic character and liposolubility of the molecule in crossing cell membrane of the microorganism, and hence enhances the biological utilization ratio and activity of the testing drug/compound (Graphic 1). The observed trend to antibacterial activity in all microorganism is not similar because of variant liposolubility of complexes for different bacteria [59].

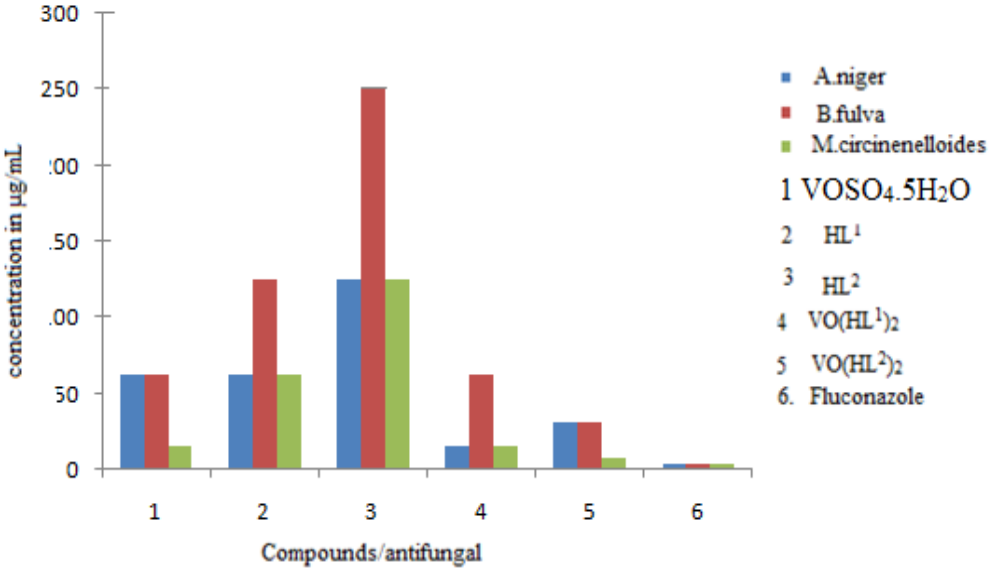
3.10 Antifungal activity

The potassium 4-nitrobenzohydroxamate and 2-chloro-4-nitrobenzohydroxamate ligands and $VO(4\text{-}NO_2C_6H_4CONHO)_2$ (I) $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_3CONHO)_2$ (II) 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 the fungi under study 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. Analysis of data has shown that potassium 4-nitrobenzohydroxamate inhibit fungi at lower concentration 62.5 for *A. niger*, *M. circenelloides* and 125µg /mL for *B. fulva* compared to potassium 2-chloro-4-nitrobenzohydroxamate which inhibits *A. niger and M. circinelloides* at 125 µg/mL and *B. fulva* at 250 µg/mL. Complex (I) has improved antifungal activity against *A. niger and M. circinelloides*. Complex (I) inhibits *A. niger and M. circinelloides* at 15.62 µg/mL.

Complex (II) has shown pronounced activity at 7.81 µg/mL against *M. circinelloides*. Although the antifungal acivity of complexes is less than standard fungicide, yet it is quite promising compared to other oxidovanadium(IV) complexes (Graphic 2). Complex $VO(2\text{-}Cl\text{-}4\text{-}NO_2C_6H_4CONHO)_2$ inhibits *M. circinelloides* at significant lower concentration.



Graphic1



Graphic 2

Table 4: *In vitro* antibacterial activities of bis(hydroxamato)oxidovanadium(IV) Complexes

Ligand/Complex	Bacteria					
	E.coli	*S.aureus*	*S.typhi*	*S.paratyphi*	*S.epidermidis*	*K.pneumonea*
$VOSO_4.5H_2O$	250	250	250		250	250
(KHL^1)	250	125	125	250	250	250
(KHL^2)	125	62.50	3.9	125	125	125
$[VO(HL^1)_2]$	31.25	31.25	62.5	62.5	7.81	62.5
$[VO(HL^2)_2]$	15.62	31.25	3.9	7.81	62.5	62.5
Standard Drug Tetracyclin Hydrochloride	15.62	15.62	7.81	15.62	15.62	15.62

Table 5: *In vitro* antifungal activities of bis(hydroxamato)oxidovanadium(IV) Complexes

Ligand/Complex	Fungi		
	A.Niger	*B.Fulva*	*M.circinelloides*
$VOSO_4.5H_2O$	62.5	62.5	15.62
(KHL^1)	62.5	125	62.5
(KHL^2)	125	250	125
$[VO(HL^1)_2]$	15.62	62.25	15.62
$[VO(HL^2)_2]$	31.25	31.25	7.81
Standard Drug Fluconazole	3.9	3.9	3.9

CONCLUSION

The bis(hydroxamato)oxidovanadium(IV) complexes derived from potassium 4-nitrobenzohydroxamate and potassium 2-chloro-4-nitrobenzohydroxamate ligands have been synthesized and characterized thoroughly by various spectral studies. The bidentate nature of hydroxamate ligands involving coordination through hydroxylamine oxygen (-NHO) and carbonyl oxygen (C=O) and a square pyramidal geometry around vanadium has been inferred from spectral studies. The electrochemical study has 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 relative to standard drug compound. The complexes derived from 2-chloro-4-nitrobenzohydroxamate ligands have shown pronounced antimicrobial activity than 4-nitrobenzohydroxamate analogue.

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