

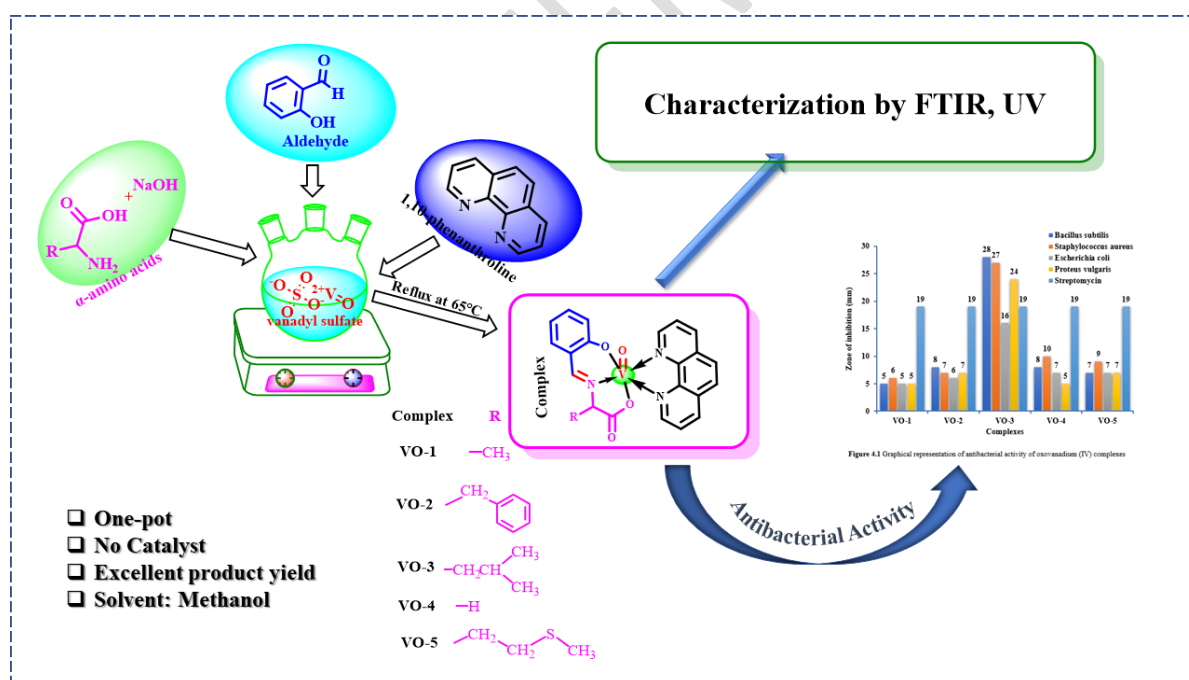
Synthesis, and In-vitro Antibacterial Activity Studies of Characterization Oxovanadium (IV) Complexes of α -Amino Acid Schiff Bases and 1,10-Phenanthroline Ligands

Abstract

Oxovanadium(IV) complexes of the type $[\text{VO}(\text{L})(\text{phen})]$ (VO-1 to VO-5) have been synthesized and characterized by FTIR and UV-Vis spectra, molar conductance, melting points, and magnetic susceptibilities measurements, where L= N-salicylidene- β -alanine (sal-ala), N-salicylidene-glycine (sal-gly), N-salicylidene-DL- β -phenylalanine (sal-pheala), N-salicylidene-leucine (sal-leu), and N-salicylidene-DL-methionine (sal-met), and phen is 1,10-phenanthroline. The infrared spectral data reveals that the tridentate nature of the amino acid-based Schiff base ligand and the coordination of the ligand through azomethine nitrogen, phenolic oxygen and carboxylate oxygen with vanadyl (VO^{2+}) ion. All of these complexes were determined to be non-electrolyte in nature, according to conductivity measurements. The magnetic moment measurements have been attributed that these complexes are paramagnetic and have d^1 configuration of vanadium (IV) ion. The antimicrobial activity of the synthesized complexes was evaluated against four pathogenic bacteria viz. *Escherichia coli*, *Proteus vulgaris*, *Bacillus subtilis* and *Staphylococcus aureus*.

Keywords: α -Amino Acid; Oxovanadium (IV) complexes; Schiff base; 1,10-phenanthroline.

Graphical abstract :



1. Introduction

Schiff base complexes of amino acids have garnered a significant amount of attention in recent years due to the physiological and pharmacological activity that they exhibit [1,2]. Schiff bases maintain a significant role in metal coordination chemistry as they facilitate the incorporation of transition metals. This is attributed to their ability to serve as ligands, forming stable complexes with metal ions. This phenomenon leads to an elevation in the ligand's biological activity and a reduction in the cytotoxic impacts of the metal ion and ligand upon the host [3].

In the past decade, numerous vanadium complexes featuring organic chelating ligands have undergone evaluation in animal and cell models, aiming to enhance both absorption and tissue uptake [4,5]. Vanadium possesses biological, medicinal [6], and pharmacological [7] significance in different forms [8,9]. The coordination chemistry of vanadium has garnered considerable interest owing to the use of diverse vanadium complexes as templates for understanding the biological roles of vanadium [10-13]. These roles encompass a spectrum of activities, including antimicrobial [14], antitumor [15], antioxidant [16], and anti-diabetic properties [17,18]. Additionally, vanadium complexes have been implicated in nitrogen fixation [19], phosphorylation [20], insulin mimicking [21-25], haloperoxidation [26], inhibition of tumor growth, and prevention of carcinogenesis [27]. Furthermore, high-valent vanadium complexes are being explored as innovative catalytic reagents in various oxidation reactions [28,29], such as olefin oxidation [30,31], sulfides [34,35], benzene/alkyl aromatic compounds [32,33], and alcohols [36-38]. Due to their potential applications, vanadium complexes have garnered significant attention in interdisciplinary research, especially regarding their synthesis and design for addressing various medical conditions [39, 40]. The configuration of the oxovanadium (IV) complex is greatly influenced by the chelating abilities of its ligands, as demonstrated in existing literature [41]. Based on reports, Schiff bases demonstrate the capacity to establish stable complexes with vanadium, commonly featuring coordination numbers ranging from four to six. [42]. Four and five-coordinate complexes may display geometries such as distorted square pyramidal, or distorted trigonal bipyramidal, square pyramidal arrangements. Regarding six-coordinate complexes, distorted octahedral structures have been observed, typically with an oxygen atom occupying the apical position. [43-45].

We recently conducted a study where we synthesized and characterized five new mixed ligand oxovanadium complexes. These complexes contained a Schiff base derived from salicylaldehyde and different amino acids (N-salicylidene- β -alanine, N-salicylidene-glycine, N-salicylidene-leucine, N-salicylidene-DL- β -phenylalanine, and N-salicylidene-DL-methionine) along with 1,10-phenanthroline. We then tested the antimicrobial activities of these complexes against pathogenic bacteria including *Escherichia coli*, *Proteus vulgaris*, *Bacillus subtilis*, and *Staphylococcus aureus* in a laboratory setting.

2. Experimental Methods

All chemicals and solvents were reagent grade and were used as received without further purification. The amino acid-based Schiff base tridentate ligands were synthesized according to published literature. The polypyridyl ligands 1,10-phenanthroline are commercially available. These complexes were synthesized by the template method.

Infrared spectra were recorded on a FTIR-8400, SHIMADZU, Japan using a KBr disc, at the Central Science Lab of Rajshahi University, UV-visible spectra of complexes were recorded on a SHIMADZU DOUBLE BEAM spectrophotometer (model UV-1200) at the Department of Chemistry, Rajshahi University. The melting points or decomposition temperature of all the prepared metal complexes were observed with an electrothermal melting point apparatus. It was, however, not possible to measure the melting points beyond 300°C. The conductance measurements were made at room temperature using a WPACM35 conductivity meter and a dip-cell with a platinized electrode. The SHERWOOD SCIENTIFIC magnetic susceptibility balance was used to probe the magnetic nature of the complexes.

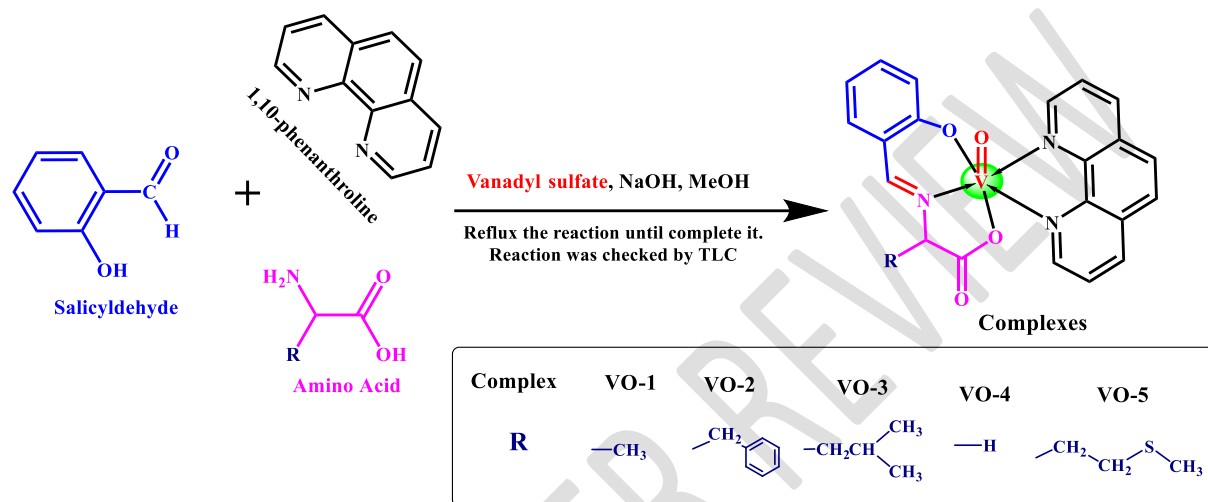
2.1 Procedure for the Synthesis of the complexes

2.2.1 Preparation of $[VO(sal-ala)(phen)]$, (VO-1)

For the preparation of oxovanadium (IV) complexes, a round bottom flask containing a methanolic solution of salicylaldehyde (sal) (0.3 mL, 3 mmol) was filled with a mixture of α -amino acids, β -alanine (ala) (0.267 g, 3 mmol), and NaOH (0.100 g, 2.25 mmol) in 10 mL methanol. After refluxing the resultant solution for an hour, vanadyl sulphate (0.489 g, 3 mmol) was added in a methanolic solution. After refluxing the mixture for an hour, a pale blue precipitate formed. To this mixture 1,10-phenanthroline (phen) (0.595 g, 3 mmol) taken in 10 mL of methanol was added. The solution on further refluxing for 1 hour gave a red

precipitate. The precipitate was filtered off on a Buchner funnel, washed with methanol and finally dried in a vacuum desiccator over anhydrous CaCl₂. [46]

Complexes VO-2 to VO-5 were prepared by the procedure as described for complex VO-1 using DL-β-phenylalanine (phyala) (0.495 g, 3 mmol); leucine (leu) (0.393 g, 3 mmol); glycine (gly) (0.225 g, 3 mmol); DL-methionine (met) (0.448 g, 3 mmol) respectively instead of β-alanine (ala).



Scheme 1: Preparation of the proposed Oxovanadium complexes, VO-1 to VO-5

2.1.2 Physical, Analytical and Spectral Data of synthesized complexes, VO-1 to VO-5

[VO(sal-ala)(phen)], (VO-1)

Yield: 0.912 g (69%) $\Lambda_M = 17.6 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in DMF at 31 °C. IR (KBr phase, cm⁻¹): 3434br, 1625s, 1542s (C=N), 1318m, 965s (V=O), 623s, 460m (br, broad; vs, very strong; s, strong; m, medium; w, weak). UV-Vis (DMSO), λ/nm ($\epsilon/\text{M}^{-1} \text{ cm}^{-1}$): 266–306 (3215–3325), 364 (2709), 384sh (2647), 462 (329) (sh, shoulder). $\mu_{\text{eff}} = 1.89$ B.M. at 303 K. Elemental analysis (%): Calculated (Found): C: 60.28 (60.20), H: 3.91(3.74), N: 9.59(9.45), O: 14.60(14.48).

[VO(sal-pheala)(phen)], (VO-2)

Yield: 1.102 g (71%) $\Lambda_M = 16.3 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in DMF at 31 °C. IR (KBr phase, cm⁻¹): 3429br, 1620s, 1540s (C=N), 1310w, 956s (V=O), 619s, 446m. UV-Vis (DMSO), λ/nm ($\epsilon/\text{M}^{-1} \text{ cm}^{-1}$): 264–291 (3414–3311), 322 (469), 383sh (2647), 458 (96). $\mu_{\text{eff}} = 1.56$ B.M. at

303 K. Elemental analysis (%): Calculated (Found): C: 65.37 (65.12), H: 4.11(4.01), N: 8.17(8.10), O: 12.44(14.32)

[VO(sal-leu)(phen)], (VO-3)

Yield: 0.989 g (68%) $\Lambda_M = 15.1 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in DMF at 31 °C. IR (KBr phase, cm^{-1}): 3425br, 1651m, 1535m (C=N), 1326w, 963s (V=O), 619m, 453w. UV-Vis (DMSO), λ/nm ($\epsilon/\text{M}^{-1} \text{ cm}^{-1}$): 273–304 (3957–3675), 364 (2094), 388sh (2402), 456 (350). $\mu_{\text{eff}} = 1.51$ B.M. at 303 K. Elemental analysis (%): Calculated (Found): C: 61.54 (61.20), H: 4.95(4.68), N: 8.97(8.75), O: 13.66(13.48).

[VO(sal-gly)(phen)], (VO-4)

Yield: 0.644 g (50%) $\Lambda_M = 16.6 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in DMF at 31 °C. IR (KBr phase, cm^{-1}): 3382br, 1625m (C=N), 1535w, 1315w, 1107w, 960m (V=O), 849s, 618w, 440w. UV-Vis (DMSO), λ/nm ($\epsilon/\text{M}^{-1} \text{ cm}^{-1}$): 267–304 (3263–3374), 361 (1747), 383sh (2069), 466 (266). $\mu_{\text{eff}} = 1.60$ B.M. at 303 K. Elemental analysis (%): Calculated (Found): C: 58.26 (58.12), H: 3.67(3.54), N: 10.19(10.10), O: 15.52(15.32).

[VO(sal-met)(phen)], (VO-5)

Yield: 0.966 g (64%) $\Lambda_M = 8.1 \text{ ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in DMF at 31 °C. IR (KBr phase, cm^{-1}): 3401br, 1618s, 1535s (C=N), 1310m, 960vs (V=O), 618m, 449m. UV-Vis (DMSO), λ/nm ($\epsilon/\text{M}^{-1} \text{ cm}^{-1}$): 269–306 (3325–3436), 362 (2874), 396sh (2937), 475 (564). $\mu_{\text{eff}} = 1.89$ B.M. at 303 K.

3. Results and Discussion

For the purpose of determining the formation of the complexes, a variety of methods are utilized. These techniques include magnetic susceptibility, conductivity evaluation, infrared spectra, and ultraviolet-visible spectra.

3.1 Physical Properties

All the complexes of oxovanadium (IV), (VO-1 to VO-5) are soluble in DMF and DMSO but insoluble in common organic solvents such as methanol, ethanol, benzene, chloroform. The molar conductance of the complexes measured in DMF at 10^{-3} M concentration fall in the range of 8.1 to $17.6 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$. These values are lower than expected for an electrolyte. Thus, molar conductance values indicate that the complexes are non-electrolyte in nature as expected. [47] The magnetic moments of complexes were in the range 1.51–1.89 B.M., which correspond to a single electron of the d^1 system of oxovanadium (IV) center and paramagnetic in nature. [48]

Table 1 Physical Properties of the prepared oxovanadium (IV) complexes

Symbol	Complex	Color	Melting point or Decomposition $^{\circ}\text{C}$	Solubility		Conductivity $\text{ohm}^{-1} \text{ cm}^2 \text{ mol}^{-1}$	μ_{eff} in B.M
				DMF	DMSO		
VO-1	[VO(sal-ala)(phen)]	Orange	230–233 (de)	+ve	+ve	17.6	1.89
VO-2	[VO(sal-pheala)(phen)]	Orange	199–202 (de)	+ve	+ve	16.3	1.56
VO-3	[VO(sal-leu)(phen)]	Red	263–267(de)	+ve	+ve	15.1	1.51
VO-4	[VO(sal-gly)(phen)]	Blackish red	210–212 (de)	+ve	+ve	16.6	1.60
VO-5	[VO(sal-met)(phen)]	Red	258–261 (de)	+ve	+ve	8.1	1.89

3.2 IR spectral studies

The infrared spectral analysis of oxovanadium (IV) complexes reveals a broad band ranging from 3382 to 3429 cm^{-1} , indicative of the probable existence of a water molecule in a hydrated state within the complexes. [49] There are ν (C=O) bands at $1618\text{--}1652 \text{ cm}^{-1}$ and ν (C-O) bands at $1310\text{--}1326 \text{ cm}^{-1}$ in the complexes, however these bands are much weaker than the ones seen in uncoordinated amino acids. In addition, the presence of ν (V–O) modes at approximately 618 cm^{-1} ensures that the carboxylate ion is coordinated with the central metal ion. [50] The absence of the ν (O–H) band typically observed around 3600 cm^{-1} for the

phenolic –OH group in these complexes suggests the coordination of the phenolic oxygen with the vanadyl ion. The bands observed at approximately 1540 cm^{-1} could potentially be attributed to the stretching frequency of $\nu(\text{C}=\text{N})$, which would indicate that the azomethine nitrogen and heterocyclic nitrogen are coordinated with the VO^{2+} moiety. The coordination of the azomethine nitrogen and the nitrogen from heterocyclic groups is additionally supported by the presence of $\nu(\text{V}-\text{N})$ modes in the region of $440\text{--}461\text{ cm}^{-1}$. [51]

The present oxovanadium (IV) complexes exhibit the $\nu(\text{V}=\text{O})$ stretching frequency in the $957\text{--}965\text{ cm}^{-1}$ region characteristic of metal-oxygen multiple bond, thus ruling out the possibility of polymeric nature of the complexes since the polymeric oxovanadium (IV) complexes exhibit one or more broad absorption bands below 900 cm^{-1} due to bridging vanadyl group, $-\text{V}-\text{O}-\text{V}-$. [52] The present complexes exhibit medium intense band in the region $\sim 960\text{ cm}^{-1}$ indicating the monomeric nature of the complexes. [53] The IR spectra of oxovanadium (IV) complexes (**VO-1 to VO-5**) are shown in the Figures 1-5.

Table 2 Important IR frequencies of complexes (**VO-1 to VO-5**)

Symbol	Complex	$\nu(\text{OH})$ cm^{-1}	$\nu(\text{C}=\text{O})$ cm^{-1}	$\nu(\text{C}-\text{O})$ cm^{-1}	$\nu(\text{C}=\text{N})$ cm^{-1}	$\nu(\text{V}-\text{N})$ cm^{-1}	$\nu(\text{V}-\text{O})$ cm^{-1}	$\nu(\text{V}=\text{O})$ cm^{-1}
VO-1	[VO(sal-ala)(phen)]	3434	1625	1318	1542	461	622	965
VO-2	[VO(sal-pheala)(phen)]	3429	1621	1310	1540	446	619	957
VO-3	[VO(sal-leu)(phen)]	3425	1652	1326	1535	453	618	964
VO-4	[VO(sal-gly)(phen)]	3382	1626	1315	1535	440	618	960
VO-5	[VO(sal-met)(phen)]	3401	1618	1310	1535	449	617	960

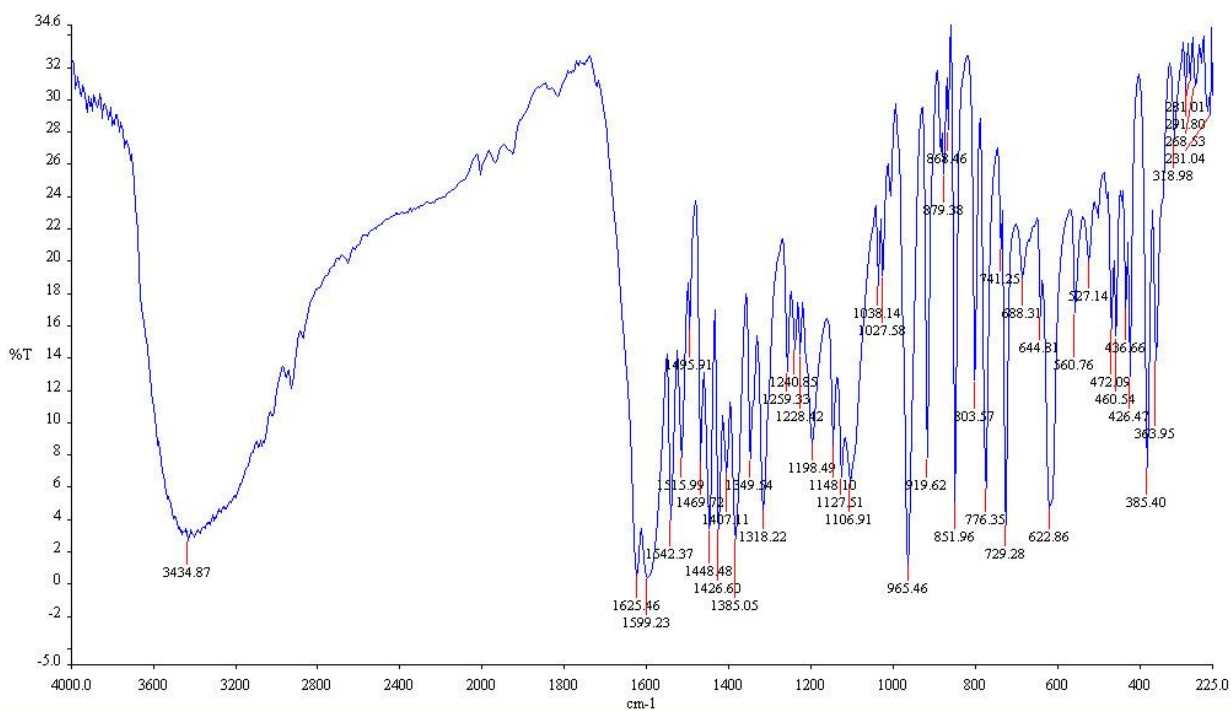


Figure 1 IR spectrum of [VO(sal-ala)(phen)] complex

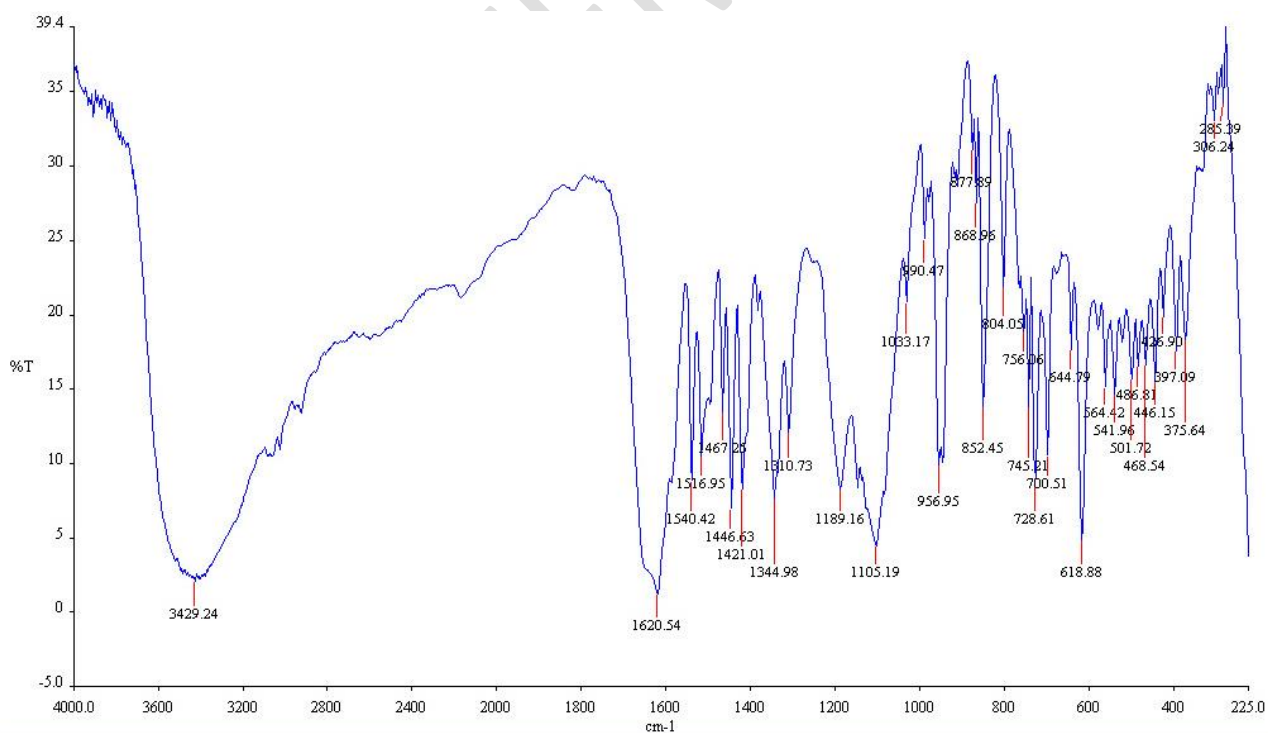


Figure 2 IR spectrum of [VO(sal-phenala)(phen)] complex

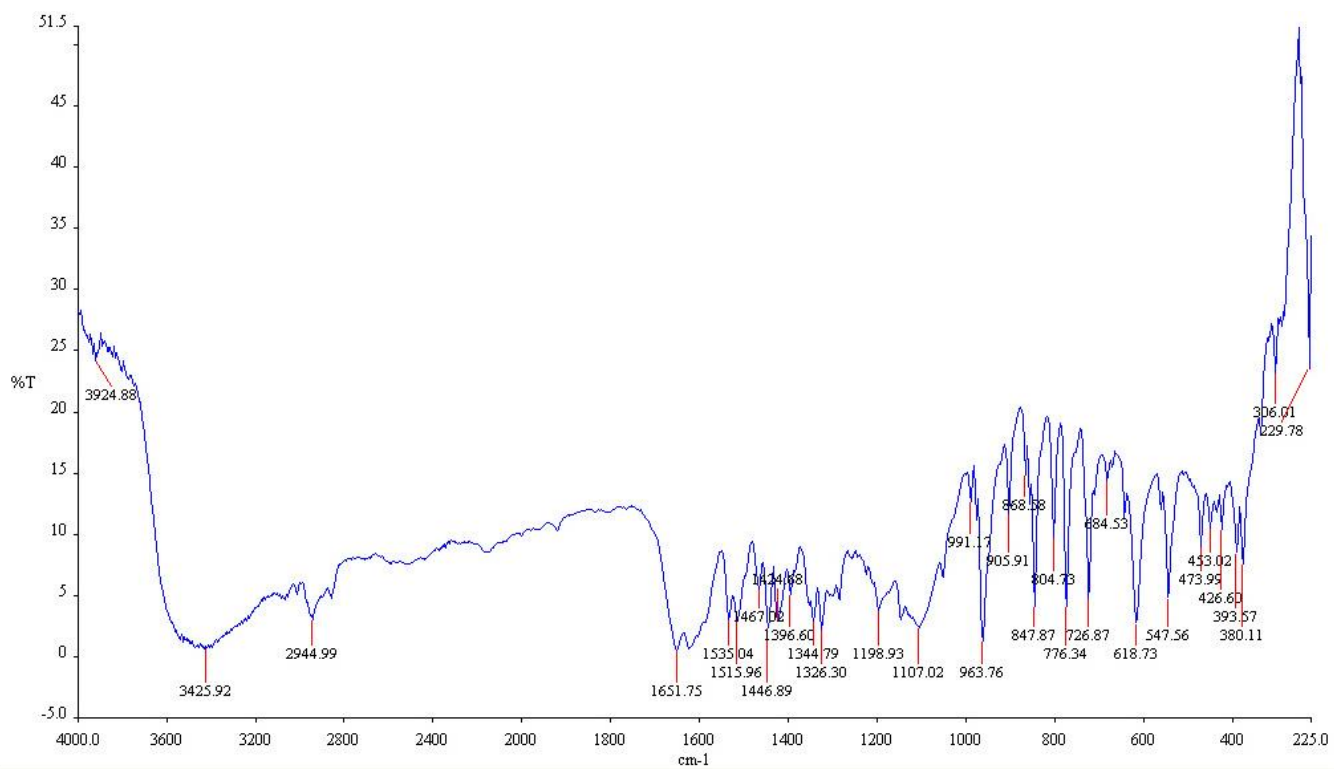


Figure 3 IR spectrum of [VO(sal-leu)(phen)] complex

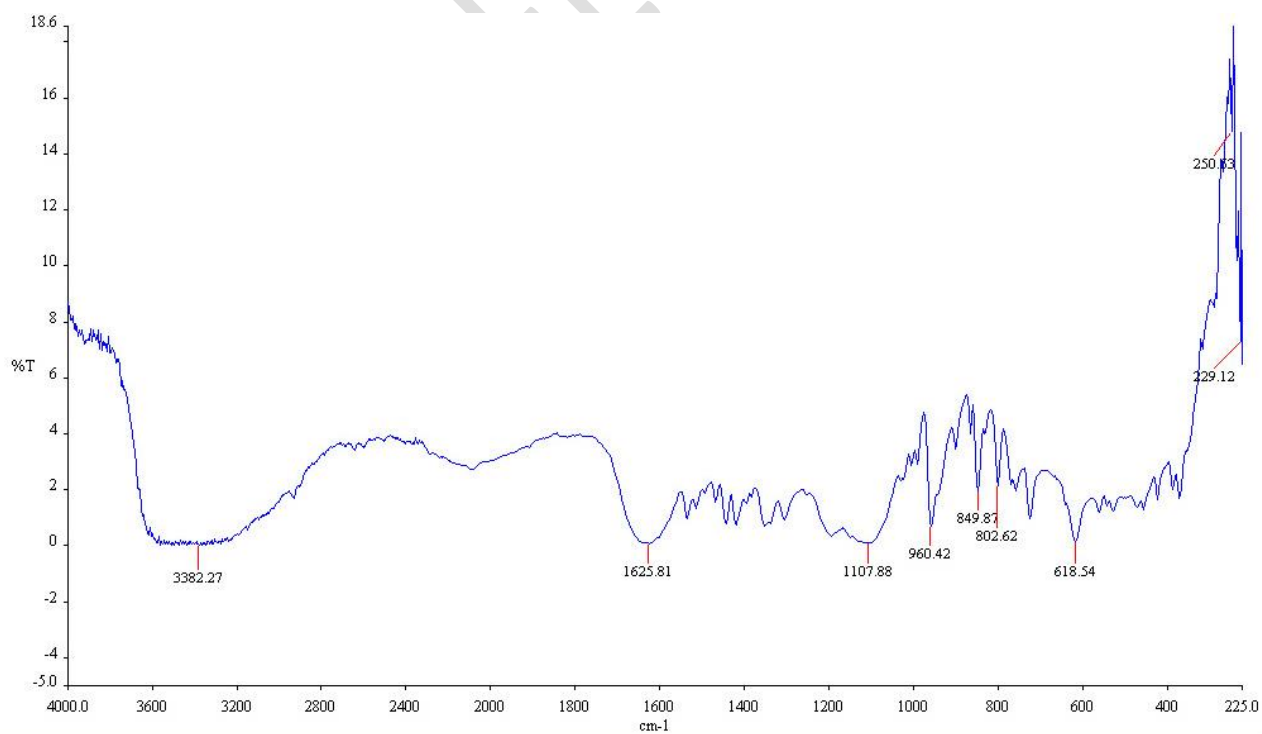


Figure 4 IR spectrum of [VO(sal-gly)(phen)] complex

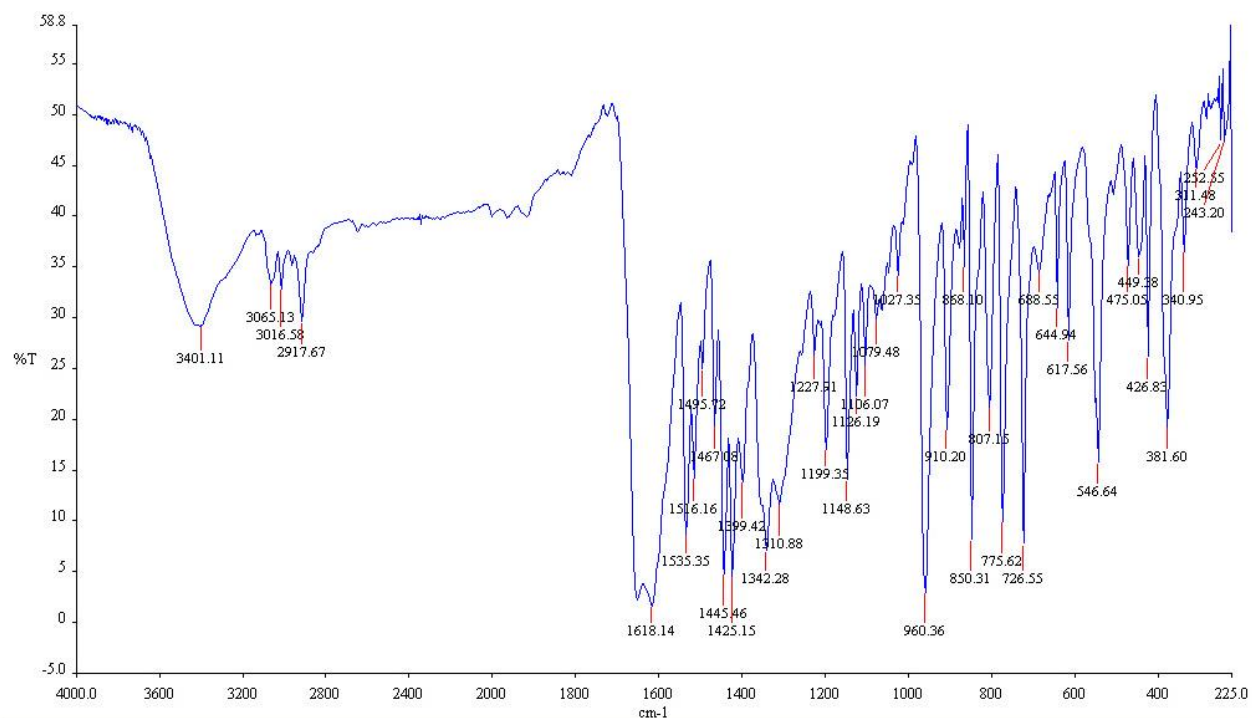


Figure 5 IR spectrum of [VO(sal-met)(phen)]complex

3.3 UV-Visible spectral analysis

At wavelengths between 200 and 800 nm, the complexes' absorption spectra were recorded in DMSO. The complexes VO-1 to VO-5 display a shoulder at around 385 nm, which can be attributed to a ligand-to-metal charge-transfer (LMCT, $\text{PhO}^- \rightarrow \text{V}$) transition. The remaining bands in the ultraviolet region are indicative of intra-ligand transitions. [54] The $\pi \rightarrow \pi^*$ transition can be attributed to the bands observed at 264–306 nm in all compounds. [55] In addition, complexes have a relatively low intensity band at approximately 460 nm, which can be attributed to the transitions between d-d transitions. UV-Visible spectra of the complexes (VO-1 to VO-5) are given in the Figures 6 – 10.

Table 3 Important UV-Visible spectra of complexes (VO-1 to VO-5)

Symbol	Complex	λ , nm (ϵ , $\text{M}^{-1} \text{cm}^{-1}$)			
VO-1	[VO(sal-ala)(bpy)]	266–306 (3215–3325)	364 (2709)	384sh (2647)	462 (329)
VO-2	[VO(sal-pheala)(bpy)]	264–291 (3414–3311)	322 (469)	383sh (874)	458 (96)
VO-3	[VO(sal-leu)(bpy)]	273–304 (3662–3325)	364 (2094)	388sh (2402)	456 (350)

VO-4	[VO(sal-gly)(bpy)]	267–304 (3263–3374)	361 (1747)	383sh (2069)	460 (266)
VO-5	[VO(sal-met)(bpy)]	269–306 (3325–3436)	362 (2874)	396sh (2937)	475 (564)

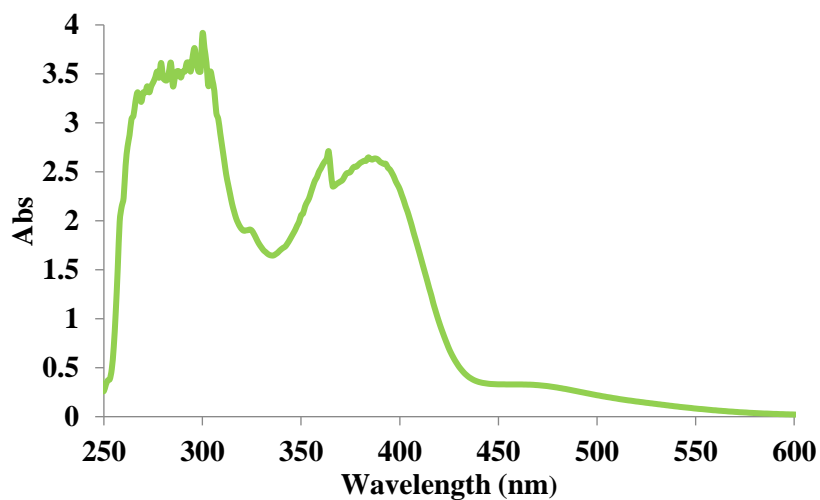


Figure 6 UV-Visible spectrum of [VO(sal-ala)(phen)] complex

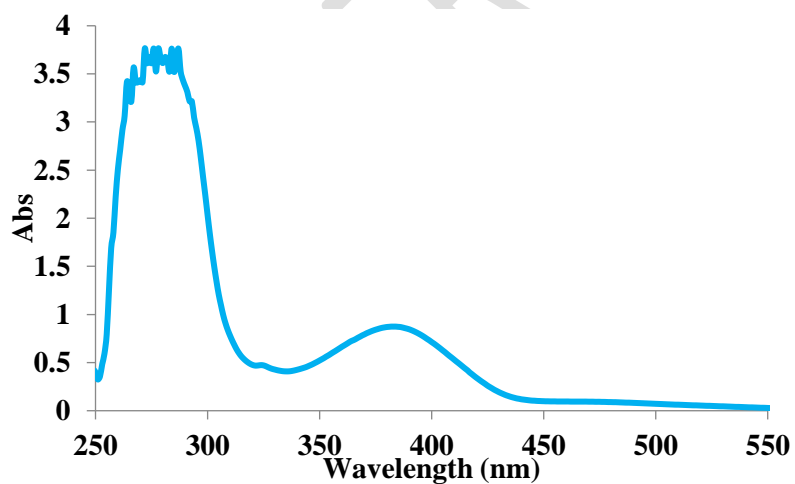


Figure 7 UV-Visible spectrum of [VO(sal-pheala)(phen)] complex

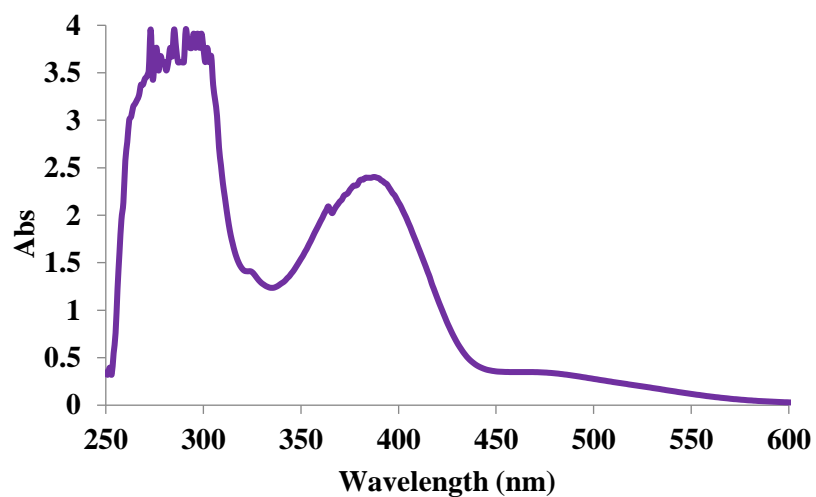


Figure 8 UV-Visible spectrum of [VO(sal-leu)(phen)] complex

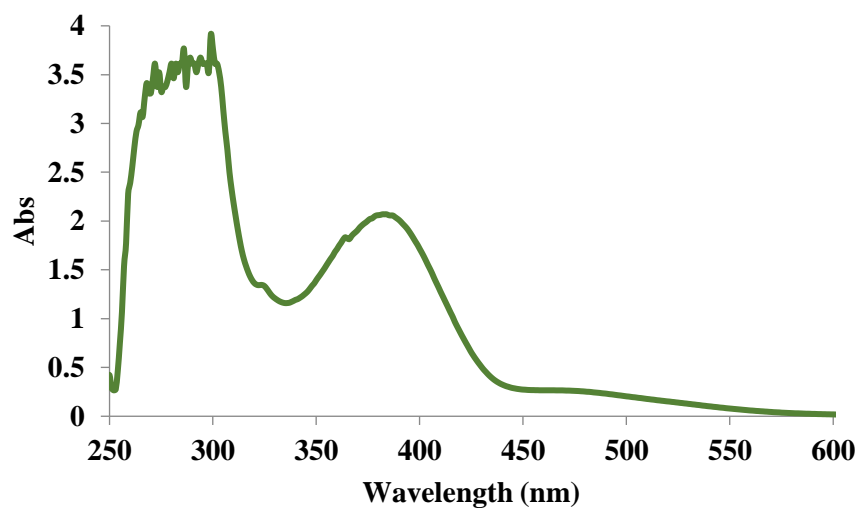


Figure 9 UV-Visible spectrum of [VO(sal-gly)(phen)] complex

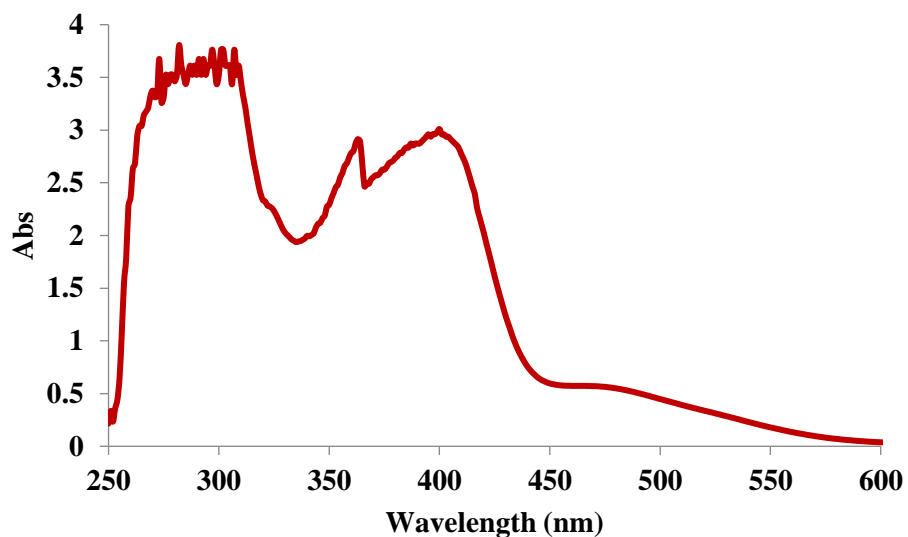
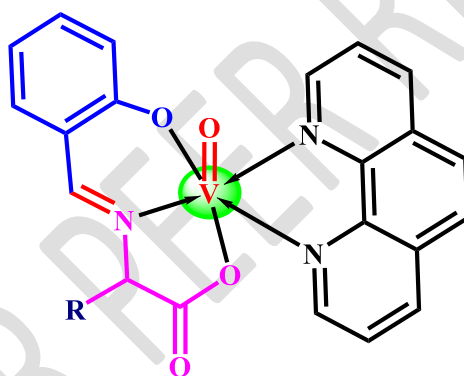


Figure 10 UV-Visible spectrum of [VO(sal-met)(phen)] complex

Based on the above characterization the presumptive structure of our synthesized complexes may be:



Complexes

Complex	VO-1	VO-2	VO-3	VO-4	VO-5
R	$-\text{CH}_3$	$-\text{CH}_2$ (benzene ring)	$-\text{CH}_2\text{CH}(\text{CH}_3)_2$	$-\text{H}$	$-\text{CH}_2-\text{CH}_2-\text{S}-\text{CH}_3$

Figure 11 Probable structure of [VO(sal-met)(phen)] complex

4. Antibacterial Activity

The antibacterial activities of the ten oxovanadium (IV) complexes were screened at the concentration of 10 $\mu\text{g}/\text{disc}$ against four pathogenic bacteria viz. *Escherichia coli*, *Proteus vulgaris*, *Bacillus subtilis* and *Staphylococcus aureus*. The results obtained were compared

with the inhibition of the standard antibiotic, streptomycin (10 µg/disc). The results are shown in the Table 4. The complexes **VO-1 to VO-5** were found to be active against all the test bacteria, with the complexes **VO-3** being even more potent than the standard against all the bacteria except for *Escherichia coli*. The activity of the complexes **VO-3** against *Escherichia coli* are comparable with the standard. The remaining complexes **VO-1, VO-2, VO-4** and **VO-5** were active with low to moderate potency against all pathogenic bacteria and in comparison, of the result of the zones of inhibition of these complexes with that of the standard, streptomycin, their activities were lower than that of standard. It may thus be concluded that the suitable choice of organic ligands coordinated to the VO²⁺ moiety influences the antibacterial activity of the individual complexes. The antimicrobial activity of the complexes may be described on the basis of their effective interaction with the microbes which cause discrete and distinct types of injuries to microbial cells as a result of oxidative stress, protein dysfunction or membrane damage. More research is needed to carry out to disclose the activity and structure relationship.

Table 4.Antibacterial activities of the oxovanadium (IV) complexes and streptomycin.

Bacterial strains		Zone of inhibition, diameter in mm					
		VO-1 10 µg/disc	VO-2 10 µg/disc	VO-3 10 µg/disc	VO-4 10 µg/disc	VO-5 10 µg/disc	Streptomycin 10 µg/disc
Gram positive	<i>Bacillus subtilis</i>	5	8	28	8	7	19
	<i>Staphylococcus aureus</i>	6	7	27	10	9	19
Gram negative	<i>Escherichia coli</i>	5	6	16	7	7	19
	<i>Proteus vulgaris</i>	5	7	24	5	7	19

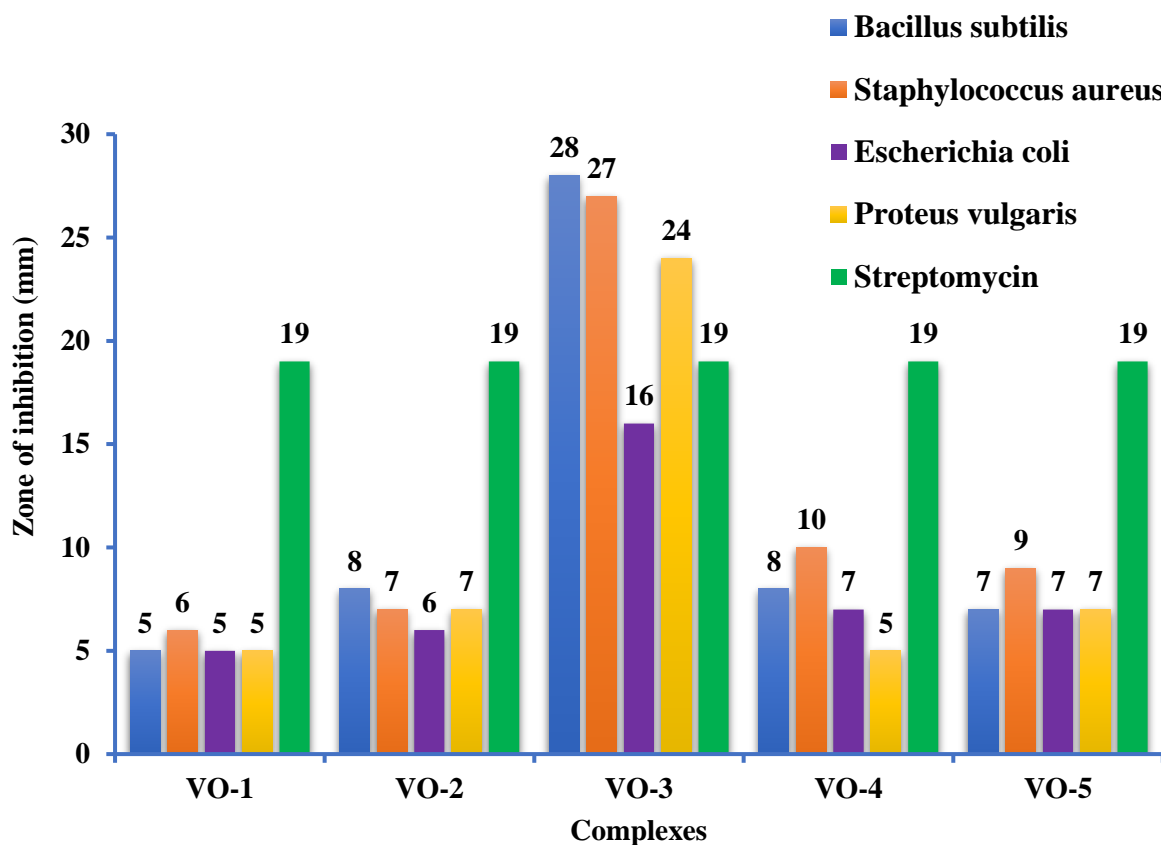


Figure 12 Graphical representation of antibacterial activity of oxovanadium (IV) complexes

Conclusions

The VO^{2+} complexes of *O, N, O*-donor α -amino acid Schiff bases and 1,10-phenanthroline have been synthesized and characterized. The analytical data reveal that the complexes are non-electrolytic and paramagnetic in nature. The magnetic moment values of the complexes are in accordance with the d^1 electronic configuration of the $\text{V}^{\text{IV}}\text{O}^{2+}$ moiety. Therefore, the structure of the complexes (**VO-1 to VO-5**) may be assigned as distorted octahedral geometry with VO_3N_3 coordination environment on the basis of physical and spectroscopic data.

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