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# A comprehensive review on the synthesis, biological applications of vanadium metal complexes

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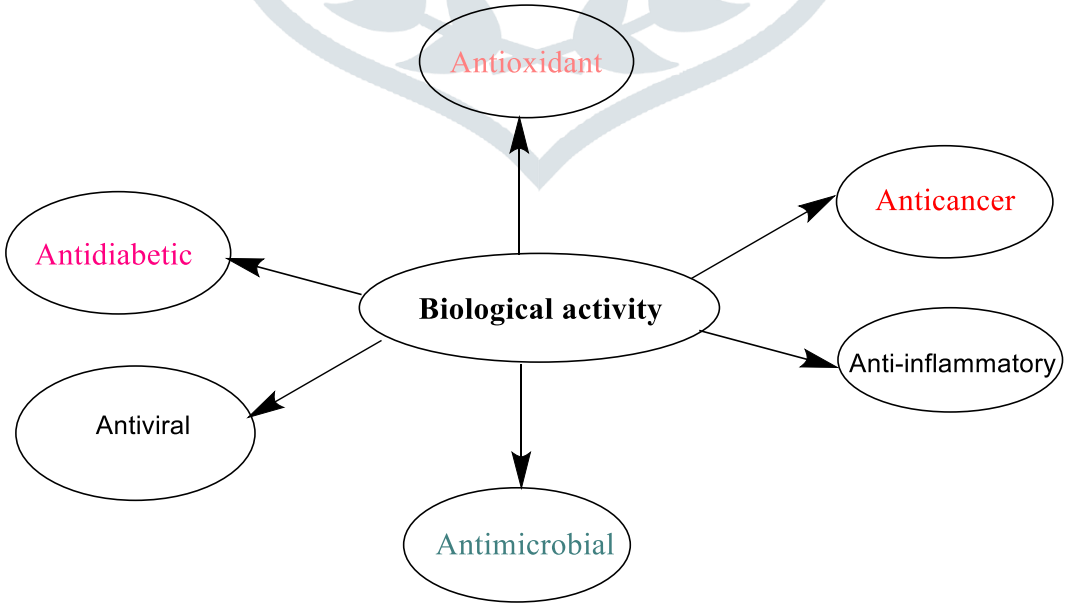
## Abstract

The study of coordinate bonds formed between ligands and central metal atom is known as coordination chemistry. Vanadium is the 22nd most abundant element in the universe and can be found in all biological systems (0.013% w/w). The two major ways through which the digestive and respiratory system of vertebrates absorbs vanadium are food consumption and air respiration. Since vanadium was discovered to be an essential trace element for certain species, interest in its coordination chemistry has increased. Vanadium compounds have gathered significant attention for a number of main reasons, especially the coordination chemistry of transition metal complexes. Here in this review article we are going to report the latest published research on vanadium based mixed ligand complexes, their characterization and structural properties along with their uses in various fields especially in medical applications, including anti-tuberculosis, antiviral, antihyperglycemic, antitumor, antioxidant, anti-inflammatory, antimicrobial, anti-fungal, anti proliferative, anticancer, and antidiabetic activities.




## Keywords

Vanadium, Biological Activity, Transition metal,Oxidation state.

## 1. Introduction:

Coordination chemistry investigates the formation of complex molecules where a central metal atom binds to surrounding molecules or ions, known as ligands. Vanadium, is crucial for various life forms, human tissues, particularly the kidney, liver, and bones.[1,2] Contain approximately 0.3 mg/kg of vanadium, with plasma concentrations around 200 nM. Dietary intake and inhalation are the primary routes of vanadium absorption in vertebrates.[3]Since vanadium has been recognized to be an important trace element for certain organisms, its coordination chemistry has drawn notable attention. For various significant reasons, vanadium compounds especially those containing oxovanadium(IV) have attracted a lot of attention.[4] β-diketones or β-dicarbonyl compounds, are an important type of molecules with two carbonyl groups linked by a methylene group. Their versatility makes them valuable substrates in organic synthesis.[5] Inspired by vanadium's biological functions and the intriguing bioactivity of β-diketones, researchers sought to combine these chemistries by developing novel vanadium-based β-diketone complexes. These complexes hold promise for exhibiting anti-tumor properties against various cancer cell lines.[6,7,8]

Vanadium plays a vital role in bioinorganic chemistry. Vanadium coordination complexes are the focus of much research due to their distinctive properties, such as availability to high oxidation states, adaptability, varied coordination numbers, and the capacity to change between oxidation states.[9] Vanadium displays a wide range of potential therapeutic applications, including anti-tuberculosis, antiviral, antihyperglycemic, antitumor, antioxidant, anti-inflammatory, antimicrobial, antifungal, antiproliferative, anticancer, and antidiabetic activities.[10-17]

## 2. Methodology

### 2.1 Search parameters

A comprehensive review of articles and literature from academic fields, official publications retrieved from the internet, and online publications is necessary to complete this study. The studies included in this paper were identified using the following search criteria: research on mixed ligand complexes of vanadium and oxovanadium with biological activity. Research on antibacterial, antituberculosis, anti-HIV, anti-chronic rheumatism, anti-tumor, antioxidant, anti-inflammatory, antifungal and anticancer aspects are discussed as biological activity.

### 2.2 Words used during the search

The following words are used during the search : mixed ligand complexes; vanadium (IV) complexes; oxo-vanadium complexes; catalyst action; oxidation; salicylaldehyde derivative; anti-diabetic substances; biological activity; fundamental characterization techniques; Schiff-base ligands; β-diketones; anticancer activities; VO(IV) complexes; monooxido vanadium(V) complexes;dioxidovanadium (V) complexes; acetylacetone, benzoylacetone, 3-methyl and 3-ethyl pentanedione.

### 2.3 Checked articles

More than sixty papers checked in overall. Six publications dealt with vanadium Schiff base complexes, twelve with β-diketone complexes of vanadium, thirteen with reviews of vanadium mixed ligand complexes, ten with biological functions on β-diketone derivatives complexes, eight with catalytic actions of Schiff base complexes, four with chemical transformations of $V^{IV}$ and $V^{V}$ complexes, and twenty with biological action on vanadium Schiff base complexes were among the studies found.

## 3. Vanadium Mixed Ligand Complexes with Biological Activity

The study of mixed ligand complexes including β-diketone derivatives, Schiff base compounds, N and O donor compounds, and others has garnered significant attention in bioinorganic chemistry. The discovery that a variety of these complexes can function as useful models for physiologically significant species is what has led to this increase in interest. Creating novel metal complexes with increased biological activity is thought to require the synthesis of vanadium metal mixed-ligand complexes. Recent advancements in medicinal chemistry and bioinorganic chemistry have significantly expanded the nation of vanadium metal ion coordination chemistry by introducing a diverse array of ligand types.

Vanadium, a transition metal, has increased significant interest in recent years due to the potential of its complexes to exhibit various biological activities. Mixed ligand complexes, where vanadium is bound to two or more different types of molecules (ligands), offer a particularly exciting avenue for research because the properties of the complex can be fine-tuned by tailoring the chosen ligands. This allows scientists to design complexes with specific biological targets in mind.

Here's a deeper dive into the research on biological activity of vanadium mixed ligand complexes:

### 3.1 Promising Applications:

**3.1.1 Antimicrobial activity:** Several studies have shown that vanadium mixed ligand complexes can be effective against various bacteria, fungi, and even tuberculosis-causing bacteria. The specific mechanism of action can vary depending on the complex, but it may involve disrupting the cell wall or interfering with essential cellular processes.

**3.1.2 Anti-cancer activity:** Vanadium complexes have shown promise in inhibiting the growth and proliferation of cancer cells. The exact mechanisms are still under investigation, but they may involve inducing cell death or interrupting signaling pathways crucial for cancer cell survival.

**3.1.3 Antioxidant activity:** Research recently showed that the antioxidant properties of some vanadium mixed ligand complexes preserve cells from the harm of free radicals. This could potentially be beneficial in conditions associated with oxidative stress, such as chronic diseases and aging.

**3.1.4 Other potential applications:** Research is ongoing to explore the potential of vanadium mixed ligand complexes for treating other conditions such as diabetes, chronic inflammation, and HIV infection.

### 3.2 Factors Affecting Biological Activity:

Vanadium mixed ligand complex biological activity is dependent upon following variables, such as:

**3.2.1 The ligand type that is used:** Different ligands can significantly influence the complex's properties, such as its charge, stability, and lipophilicity (ability to interact with fats). These factors, in turn, affect how the complex interacts with biological systems.

**3.2.2 The oxidation state of vanadium:** Vanadium can exist in different oxidation states, and each state can lead to complexes with distinct biological activities.

**3.2.3 The overall structure of the complex:** The spatial arrangement of the ligands around the vanadium center can influence how the complex interacts with biomolecules like enzymes or cell membranes.

### 3.3 Current Research and Future Directions:

Research on vanadium mixed ligand complexes is a rapidly evolving field. Scientists are continuously developing new complexes with improved efficacy and selectivity for specific biological targets. Computational modeling and advanced characterization techniques are playing an increasingly important role in this process. Here are some potential future directions for research:

**3.3.1 Designing complexes with targeted delivery:**

Developing complexes that can specifically target diseased cells or tissues could improve their effectiveness while minimizing side effects.

**3.3.2. Understanding mechanisms of action:**

A deeper understanding of how these complexes exert their biological effects is crucial for optimizing their design and potential therapeutic applications.

**3.3.3. Clinical trials:**

Promising complexes identified through pre-clinical studies will need to undergo rigorous clinical trials to evaluate their safety and efficacy in human. Studying the biological activity of vanadium mixed ligand complexes could lead to the discovery of new treatment medicines for a wide range of diseases. We should anticipate much more fascinating discoveries in this area as research in it progresses.

## 3.4 Antimicrobial activity

*Domyati, D et al*[18]synthesized mixed ligand complexes of vanadium containing derivatives of aminophenol and 4-amino-5-hydrazinyl-4H-1,2,4-triazole-3-thiol.The produced mixtures have been studied in associated with types of Gram-Negative and Gram-Positive bacteria including *Pseudomonas aeruginosa, Streptococcus pneumoniae, E. coli* and *Staphylococcus aureusin* addition to yeast, such as *Candida albicans.*

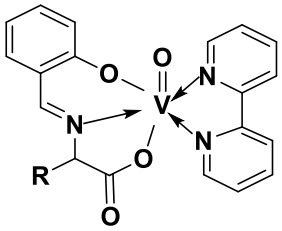
*Ramos, C. S et al*[19]synthesized Piperine, piperic acid, 3-geranyl-geranyl-4-hydroxybenzoate acid, and glutamic acid are four novel vanadium complexes that have natural biologically active ligands. The antibacterial properties of these blended ligand complexes were noted against the *E. floccosum* fungus as well as Gram+ve bacteria *Staphylococcus aureus,* enteric bacteria and Gram-ve bacteria *E. coli, Klebsiella pneumoniae,* and *P. aeruginosa* etc.

*Luo, X. Q et al*[20] prepared two new oxidovanadium(V) complexes with the deprotonated state of 3-hydroxy-2-methyl-4H-pyran-4-one and 2-hydroxybenzohydroxamate and also the dianionic form of the hydrazoneligand. The researchers examined the effects of the compounds on the antibacterial properties of the compounds against *Candida albicans, E. coli,* and *Staphylococcus aureus* (**Table 1**).

| Compounds | Staphylococcus aureus | E. coli |
|---|---|---|
| $H_2L$ | 64 | 16 |
| Complexes 1 | 2.0 | 1.0 |
| Complexes 2 | 8.0 | 2.0 |

**Table 1 Antibacterial properties oxidovanadium(V) complexes**

Oxovanadium(IV) complexes have been synthesized with bpy, sal-ala, sal-gly, sal-pheala, sal-leu, sal-met (**figure 1**) and characterized using FTIR and UV-Vis spectra. The synthesized complexes antibacterial activity was evaluated by *in vitro* experiments against different varieties of gram +ve bacteria such as *Bacillus subtilis, Staphylococcus aureus* and two gram-ve bacteria like *E. coli* and *Proteus vulgar* by *Hasan, M.A et al*[21].



**Complexes 1-5** **Structure of oxovanadium(IV) complexes**

| Complexes | 1 | 2 | 3 | 4 | 5 |
|---|---|---|---|---|---|
| R | -CH3 | -CH2-CH(-CH3)-CH3 | -CH2-C6H5 | -H | -CH2-CH2-S-CH3 |

**Figure-1** **Oxovanadium(IV) complexes with bpy, sal-ala, sal-gly, sal-pheala, sal-leu, sal-met**

*Z. A. Alkaya et al*[22] created new oxovanadium mixed ligand complexes by hydro/solvothermal synthetic techniques, derived from interactions between $V_2O_5$ and 2,6-pyridine dicarboxylic acid with water or ethanol. Newly formed complexes are characterized by thermogravimetric, XRD, and manganometric titration. The microorganisms *C. albicans, E. coli, Bacillus subtilis, Staphylococcus aureus* and *E. faecalisare* all susceptible to these complexes' antibacterial activity. *Sharma S et al*[23]prepared the tris(nicotinohydroxamato) vanadium(III) complex by the reaction of $VCl_3$ in methanol solvent under nitrogen environment with three equivalents of potassium salts of nicotinohydroxamate. Elemental analysis, molar conductivity, infrared and mass spectrum studies have been used to characterize complexes. Using the MIC method, the antibacterial properties of the newly synthesized complex were evaluated against pathogenic bacteria, like *S. aureus, E. coli, S. typhi, S. paratyphi* and *S. epidermidis* as well as fungus, including a variety of *A. niger, B. fulva*, and *M. circinelloid*. In comparison to the free ligand and metal precursor, the complex exhibited encouraging antibacterial activity.

*Schons, A.B., et al*[24]synthesized A novel oxovanadium(IV)-bis(abietate) complex was produced as a result of the synthesis, and it was examined using chemical investigation, vibrational and electronic spectra, XRD and thermal analysis. The compound $[VO(C_{20}H_{29}O_2)_2]$ with two abietate ligands was the structural formula that was discovered. When used against microbes, the VO(IV)-bis(abietate) combination shown encouraging antibacterial and antifungal action. When it came to the strains of Gram+ve bacteria like *S. aureus* , *L. monocytogenes* and Gram-ve bacteria like *Salmonella enterica Typhimurium*, the inhibitory effect showed the best results. The antifungal activity was applied to both *Candida albicans* and *Candida tropicalis*.

*Priya, B., et al*[25] have synthesized new oxidovanadium(IV) complexes by reactions between acetylsalicylhydroxamic acid with $VOSO_4.5H_2O$ and $[VO(acac)_2]$ in an absolute ethanol solvent at a 1:2 molar ratio. In addition to elemental investigations, molar conductivity, and magnetic moment measurements, the compounds are characterized by FTIR, UV–visible and Electron Spain Resonance. Vanadium is surrounded by a deformed square pyramidal geometry. The compounds exhibit noteworthy antibacterial properties in comparison to the standard medicines, fluconazole and tetracycline hydrochloride.

*Kumar, H., et al*[26] produced a new series of VO(IV) complexes of tetraazamacrocyclic in the presence of oxovanadium (IV) sulphate in $CH_3OH$ solvent with 1,8-diaminonaphthalene and substituted β-diketones ligands. Complexes were described using spectrum data, conductance measurements, magnetic characteristics, and elemental studies as sources. The spectrum studies for the oxovanadium(IV) complexes confirm a square pyramidal shape. The antimicrobial and antifungal properties of the oxovanadium complexes against *Aspergillusniger* and *Candida albicans*, as well as against *Bacillus subtilis*, *Staphylococcus aureus*, and *Escherichia coli*, were verified. When compared to the common antibiotic tetracycline and the antifungal medication fluconazole, the complexes exhibit moderate to decent activity.

*Sharma, S., et al*[27] have produced the oxidovanadium(IV) complex by the condensation reaction of $VOSO_4{\cdot}5H_2O$ and potassium 4-nitrocinnamohydroxamate in methanol-water solution. Elements analysis, molar conductivity, FTIR, UV-Vis, EPR spectrum and mass spectrometry are used to characterize the complex. It has been determined that the hydroxamate ligand is bidentately linked by hydroxamic and carbonyl oxygen atoms, involving O,O-coordination. The complex is shown to exist as a monomer by the mass spectra, EPR, and magnetic susceptibility, and a distorted square pyramidal shape is suggested to surround vanadium. These complexes show biological activity against a range of pathogenic bacteria, including *E. Coli, S. Aureus, S. paratyphi, S. epidermidis*, and *K. pneumonia*, as well as fungi, including *C. albicans, B. fulva,* and *F. oxysporum*. The complexes showed increased antibacterial activity in comparison to vanadyl sulphate and the free ligand.

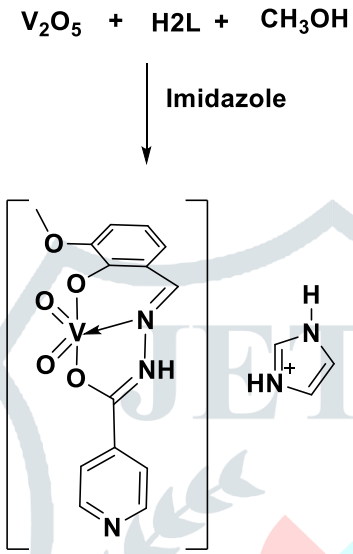
*Alghamdi, H., et al*[28] created and evaluated novel Dioxovanadium(V) complexes with the ligands 2-(5-phenyl-1,3,4-oxadiazole-2-yl)phenol and oxadiazole derivative to determine their antibacterial activity. The octahedral geometrie of vanadium ion is produced by the coordination of both bidentate and tetradentateoxadiazole ligands through the nitrogen and oxygen atoms. The examined complexes were considered for antimicrobial vise four strains of bacterial and one strain of fungal. These complexness showed the highest antibacterial potency via the *Staphylococcus aureus*.*Munawar, K.S., et al*[29]synthesized the oxidovanadium(IV) complexes by the reduction reactions of 3-(trifluoromethyl)benzenamine with benzaldehyde derivative and 2-hydroxy-1-naphthaldehyde with vanadyl(V) isopropoxide. The produced compounds were examined using thermogravimetry, FT-IR, multinuclear NMR spectroscopies and magnetic susceptibility tests. The hypochromicity seen during UV–visible spectroscopic investigations served as a clue to identify the complexes' intercalation method of interaction with Salmon sperm DNA. With a few notable exceptions, all of the synthesized precursors and complexes were classified based on their hemolytic, antibacterial, alkaline phosphatase inhibition, and insulin-mimetic activity.

## 3.5 Antidiabetic activity

*Zahirović, A et al*[30] synthesized the Vanadium (IV) complex using 5-chloro-salicylaldehyde and 2-furoic acid hydrazone was identified. In both healthy and diabetic Wistar rats, the effects of the complex's *in vivo* administration on a few metabolic measures were examined. Moderate hypoalbuminemia was found to be related with a strong antidiabetic impact.

The mixed ligand complexes of 3,6-dithio-1,8-octanediolatooxidovanadium(IV) with an $S_2O_2$ coordination mechanism have been synthesized by *Lima et al.*[31] The $S_2O_2$ donor ligand-containing oxidovanadium(IV) complex possesses excellent antidiabetic qualities that eradicate diabetes mellitus symptoms and associated comorbidities. *Naglah AM et al*[32] synthesized Six novel insulin-mimetic vanadyl(IV) injections. These compounds were created by equal molar ratio reactions between AA, $VOSO_4$, and FA in neutralized medium. Ile, Thr, Pro, Phe, Lys and Gln are the amino acids. These complexes' ability to prevent diabetes was tested in male albino rats that had been streptozotocin-induced diabetics. Lipid profile, blood glucose and insulin levels, liver and kidney functions, and SOD antioxidant are validated factors of the effectiveness of VO(IV)/FA/AAn system chemicals as antidiabetic pharmacological agents.

*Patel N et al*[33]synthesized dioxidovanadium(V) mixed ligand complexes by using imidazoles or their derivatives (**Figure 2**) and the hydrazone Schiff base ligand isonicotinic acid (2-hydroxy-3-methoxy-benzylidene)-hydrazide ligand.(**Scheme 1**) Inhibition techniques for, α-amylase, β-glucosidase, and α-glucosidase were also used to investigate the antidiabetic features of complexes.




**Scheme 1** **Synthesis of dioxidovanadium(V) mixed ligand complexes by Patel N et al33**

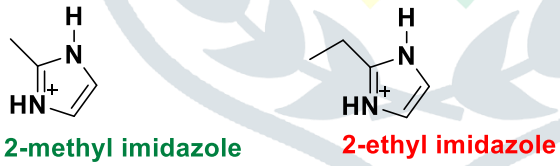



**Figure-2** **Imidazoles and its derivatives for synthesis of dioxidovanadium(V) mixed ligand complexes**

*Ahmed, S., et al*[34]synthesized and characterized novel heterolepticoxovanadium(IV) complexes including diclofenac and ligands based on thiosemicarbazone (TSC). Using enzymes for example α-amylase and α-glucosidase the complexes *in vitro* antidiabetic efficacy was verified. Because methyl groups have the ability to donate electrons, complexes containing methyl substituents were more active than those containing nitro substituents. Applying molecular dynamics simulations, the dynamic behaviour of the suggested complexes was examined.

*Zahirović, A., et al*[35]prepared five new octahedral paramagnetic mononuclear oxidovanadium(IV) complexes that are neutral heteroleptic were obtained through solution synthesis. Elemental analysis, IR, NMR, and EPR spectroscopy, cyclic voltammetry were applied to carry out the characterisation process. Investigated were the

effects of the complexes *in vivo* administration on a few metabolic parameters in Wistar rats both diabetic and healthy. There was a significant strong antidiabetic effect related to moderate hypoalbuminemia.

Single-crystal X-ray, physicochemical, and spectroscopic techniques were used to isolate and characterize oxidovanadium(IV) and oxidovanadium(V) complexes with tridentate Schiff base ligands based on 5-sulfosalicylaldehyde, 5-nitrosalicylaldehyde or 5-methoxysalicylaldehyde and corresponding hydrazide. The biological activity investigations included cytotoxicity tests, glucose uptake in myocytes and adipocytes, studies on myocyte C2C12 and human hepatocyte $HepG_2$ cell lines have been studied by *Szklarzewicz, Jet al.*[36]

*Patel, N., et al*[37]reported the synthesis of $VO_2(V)$ complexes which include nicotinic acid and tridentate ligand, have been studied to substantiate the following: 2-hydroxy-3-methoxy-benzylidene)-hydrazide, imidazole, and methylimidazole. Taking single-crystal X-ray analysis, the crystalline structures of complexes were determined. Complexes electrochemical characteristics as well as their UV–visible and infrared spectra were described. Investigations have also been conducted on the complexes' antidiabetic properties. Their potential as insulin enzyme inhibitors has been enhanced by their anti-diabetic properties, such as α-amylase and α-glucosidase inhibition investigations.

*Ghosh, C., et al*[38] synthesized a family of dioxidovanadium(V) complexes. The structure of complexes is $[Na(H_2O)_x]^+[V^VO_2(HL^{1-4})]^-$ where x = 4, 4.5 and 7 and $HL^{1-4}$ are 2-hydroxy-5-chloroacetophenone, 2-hydroxy-5-methylacetophenone, 2-hydroxy-5-methoxyacetophenone and 2-hydroxyacetophenone and the complexes is characterized by analytical and spectral methods. These compounds demonstrated potential effects on erythrocyte carbonic anhydrase enzymatic activity in both type 1 and type 2 diabetic patients, suggesting potential antidiabetic efficacy against T2 diabetic mice. The complexes with 2-hydroxy-5-chloroacetophenone show highest antidiabetic activity.

Rapidly and qualitatively synthesized Potential anti-diabetic candidate [VO(IV)HBDB], using HBDB of the mode N, N′-bis (2-hydroxy benzylidene)-1,2-diaminobenzene/Salophen, a well-known Schiff base with a wide range of properties. There were reported interesting and useful facts about the complexes electronic structure, band gap energy, and physical and electrical properties. The complexes show greater antidiabetic activity with α-glucosidase enzyme than free HBDB was studied by *Gandhimathi, R., et al.*[39]

## 3.6 Anticancer activity

*Levina A., et al*[40]synthesized two Vanadium(V) complexes, Using N-(salicylideneaminato)-N′-(2-hydroxyethyl)-1,2-ethanediamine ($H_2$shed), 3,5-di-tert-butylcatechol ($H_2$dtb) and 1,2-catechol (H2cat). Possible candidates for further development as intratumoral injection-delivered anticancer drugs include complexes containing $H_2$shed and $H_2$dtb.When tested against triple-negative human breast cancer (MDA-MB-231) cells, both complexes exhibited strong antiproliferative properties, but their processes varied greatly.

*Ribeiro, N.,et al*[41] prepared and characterized A series of oxidovanadium(IV) complexes. These compounds are produced from benzylhydrazides and 2-carbaldehyde-8-hydroxyquinoline with altered substituent at the p-position. Mass spectrometry, UV-visible absorption, elemental analysis, FTIR, EPR, and DFT mathematical techniques were used to identify the compounds. Compound was assessed in lung (A-549) and malignant melanoma (A-375) cancer cells.

*Alomari, F.Y., et al*[42]found that $[VO(CTZ)_2]$ $2H_2O$ complexes exhibited greater anticancer activity than the typical cisplatin chemotherapy medication. An inhibitory activity test of the complexes $[VO(CTZ)_2]$ $2H_2O$ is tested on the colon cancer cell line (HCT116). *Basaleh A.S., et al*[43]Synthesized Imidazole drug complexes made

from oxidovanadium(IV) and structurally characterized using elemental analyzer, spectroscopic methods, and thermal analysis. The synthesized complexes showed good suppression of cytotoxic activity towards both human breast cancer (HCF-7) and hepatocellular carcinoma cell lines.

*Sahu, G., et al*[44] synthesized two mixed-ligand oxidovanadium (IV) complexes and one oxidomethoxidovanadium (V) complex were synthesized. Techniques for example IR, UV-visible and HR-ESI-MS were used to characterize the ligand and complexes. Using a cell viability test against the human breast carcinoma cell MCF-7 and the non-cancerous mouse embryonic cell NIH-3T3, the anticancer potential of these complexes was evaluated.

*Ni, L., etal*[45] synthesized and characterize a dimeric mixed-ligand oxidovanadium complexes. These compounds may have strong biomolecule reactivity as potential anticancer drugs, according to tests of density functional theory. The development of HepG2 and SMMC-7721 cells was shown to be most inhibited by complexes.

*Sathiyamoorthy, B., et al*[46] synthesized the mononuclear combination of VO(II) containing the ions oxalate and ethyl-4-aminobenzoate, which was characterized based on its physical-chemical spectroscopic and bio-potential activities. Studies on elemental analysis and metal estimates for the complex verified its mononuclear nature and formula. It's IR, electronic spectra and magnetic moment further supported its geometry and ligating capability. Using the Agar well diffusion method, the complex's biopotential activities were ascertained and then juxtaposed with those of the ligand and standards, namely chloramphenicol. An in vitro study was conducted using the human breast cancer cell line MCF-7 to examine the anticancer activity of the ligand and VO(II) complex.

*Santos, T.M., et al*[47] Formed a oxovanadium complexes and the proven inhibition effect of the vanadium complex [VO(oda)(phen)] on pancreatic cancer cells autophagy mechanism. The scientific community has taken an interest in autophagy mostly due to its notable benefits over chemotherapy procedures. One of these benefits is that it targets cancer cells directly, preventing any negative effects. This is in contrast to chemotherapy, which targets tumors cells while also affecting healthy cells in the body, severely impairing patients' quality of life. Therefore, it can be said that molecular dynamics (MD) simulations are a great way to study how metal complexes interact with their biological targets. oxidovanadium(IV) complexes have been synthesized by *Ribeiro, N.,et al*[48]. Using 2-carbaldehyde-8-hydroxyquinoline and benzylhydrazides with various substituents in the para-position, the researchers created a family of benzohydrazones. A variety of analytical techniques were used to characterize each complex, including elemental analysis, mass spectrometry, FTIR, UV-visible absorption, EPR, and DFT computational approaches. All of the compounds antiproliferative properties were assessed using lung (A-549) and malignant melanoma (A-375) cancer cells.

## 3.7 Antioxidant activity

*El-Gammal, O.A., etal*[49] produced three $VO^{2+}$ compounds with $H_4$DDAT, $H_4$DDET, and $H_4$DDPT derivative. These compounds show antioxidant properties like DNA binding capacity, SOD-like activity and hydroxyl radical scavenging. *Drzezd˙ zon, J et al*[50]synthesized complex by various ligands (**Figure 3**) [VO(dipic)(phen)]·3$H_2O$, [VO(dipic)(bipy)]·$H_2O$, [VOO(dipic)](2-phepyH)·$H_2O$ and [VO(dipic)($H_2O$)$_2$]·2$H_2O$.Antioxidant qualities are demonstrated by these complexes against the superoxide anion radical. The synthetic dioxo-vanadium and oxo-vanadium complex molecules exhibited the best sensitivity towards the superoxide anion radical, as exhibited by the [VOO(dipic)](2-phepyH)•$H_2O$ complexes.

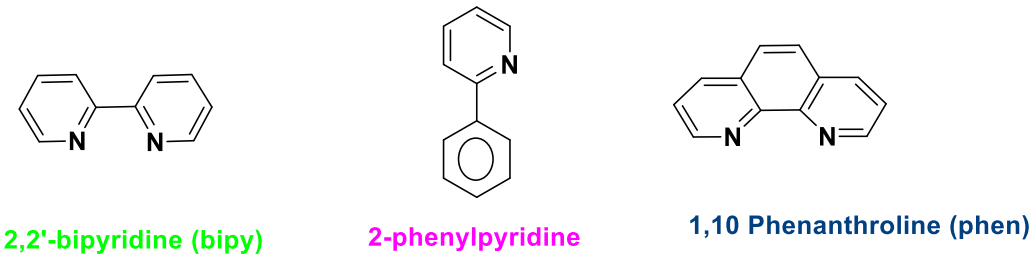



**Figure-3** **Ligands use to synthesized dioxo-vanadium and oxo-vanadium complex by Drzezd zon, J et al50**

Formation and separation of a recently created ternary Complex: V-curcumin-(2,2′-bipyridine) have been created by *Halevas E et a*[51]. Activated oxygen species reduction and decrease in cell metabolism are shown by V(IV)-curcumin.Potential application as metallopharmaceutical is proposed by the bioactivity profile of V(IV)-curcumin.

*Da Silva, T.U., et al*[52]synthesized a oxovanadium complexes [VO($L_{1-4}$)(R)] and studied using density functional theory. R refers to bipyridine, phenanthroline, and $L_{1-4}$ for the group of ligands produced from dithiocarbamate. The contribution of the L-ligand to the complexes single-occupied molecular orbital correlated with the experimental antioxidant activity ($IC_{50}$). It has been determined that the antioxidant and DNA-interaction properties of these complexes should be increased by the addition of an electron-donating substituent group (such as- $CH_3$) in the structures.

*Hasnaoui, A., et al*[53] Formed a pair of di-μ-oxidovanadium(V) complexes and examined using several spectroscopic methods. BHT and quercetin were utilised as antioxidant standards in the current investigation, and the DPPH assay was utilised to calculate the antioxidant activity of both Complexes. *Maghraoui, N., et al*[54] created two novel tetradentateoxovanadium(IV) and iron(II) Schiff base complexes in methanol. These complexes were characterized using various spectroscopic techniques, including UV–visible, FT-IR. In addition, TG and DTG were used to look into these compounds thermal stability. Lastly, the DPPH free radical scavenging assay was used to evaluate the antioxidant properties of the recently synthesized complexes. The oxovanadium complex exhibited good antioxidant activity, according to the results.

## 3.8 Antibacterial Activity

VO(IV) complex of an N,N-bis(1-naphthalidimine)-o phenylenediamine have been synthesized in 1955 by *Bendia, S. et al*[55]. Numerous physiochemical and spectroscopic methods have been used to characterize the complexes' structures. Frontier Molecular Orbitals have been applied to discuss the chemical reactivity and optimize the structure using Density Functional Theory computations. Cyclic voltammetry was used to investigate the electrochemical characteristics of the compound. Using the complex as a catalyst, cyclohexene was selectively oxidized in DMF to produce the equivalent 2-cyclohexene-1-one. Using the disc diffusion method, the antibacterial activity against two Gram positive and three Gram negative bacteria was tested. It was

discovered that the antibacterial activity against the Gram positive bacteria was greater than that against the Gram negative bacteria.

*Zandvakili, T et al*[56] created a new V(V) dimer complex was produced with BuOH and DFX and elemental analysis, $^{1}$HNMR, $^{51}$V NMR, and FTIR were used to completely characterize the product. DFX and its V(V) dimer complex were investigated for their antibacterial activities against strains of *Bacillus cereus*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*. *Zandevakili, T et al*[57] Applied the reflux technique, a novel mixed-ligand oxidovanadium (IV) complex including DFX and 1,10-phen was created. UV–Vis spectroscopy and FE-SEM were used to characterize the complex. The synthesized complex's in vitro antibacterial activity was assessed against strains of bacteria including *Pseudomonas aeruginosa*, *Bacillus cereus* and *Staphylococcus aureus*. Additionally, these compounds ability to inhibit *S. aureus* and *P. aeruginosa* biofilms was studied.

*Boucekine, I., et al*[58] produced a new NNOO-type chelate complex, by reacting bis(acetylacetonato) oxovanadium with 2 hydroxy-1-naphthaldehyde and 3,4-diaminotoluene. Elements, electronic, and infrared spectra are used to characterize the prepared compound. Taking the single-crystal XRD method, the anticipated structure was crystallized and identified. Furthermore, using DFT and TD-DFT computations in gas, we conducted a thorough study of the structural, electrical, and optical characteristics of the Oxovanadium(V), $VO^{IV}$ and $VO^{III}$ complexes. The antibacterial activity of the free ligand $H_2L$ and its corresponding VOL complex was assessed *in vitro* against strains of *Escherichia coli, Proteus mirabilis*, and *Klebseillapneumoniae*, as well as strains of *Staphylococcus aureus* and *Streptococcus pyogenes* (both Gram-positive and Gram-negative).

*Sharma, B.P., et al*[59]synthesized and characterized two new Schiff base ligands featuring 1,2,4-triazole moieties and their VO(IV) complexes. X-ray diffraction, conductivity measurement, cyclic voltammetry, electron paramagnetic resonance, Fourier transform infrared, ultraviolet–visible, and elemental analyses were used to study the ligands and their complexes. Four bacterial pathogens were examined *in vitro* using the ligands and their metal complexes: *Salmonella Typhi*, *Escherichia coli* and *Staphylococcus aureus*. *Odularu et al.*[60] told about two coordination compounds, [VO(sfz)(pl-dtc)] and [Zn(sfz)(pl-dtc)] were created using mixed ligands that included the synthesized pl-dtc crystals and sodium sulfadiazine (sfz).Characterization approaches involving physicochemical characteristics and spectral analysis (FT-IR, UV-Vis, and EPR) to confirm their syntheses and structures, structural analyses of the coordination compounds and ligands were evaluated. When compared with the ligand of pl-dtc, the coordination compounds exhibited antibacterial activities against the Gram-negative bacteria and Gram-positive bacteria respectively *Escherichia coli, Staphylococcus aureus*, according to the *in vitro* antibacterial investigations.

*Tan, X.R., et al*[61]Created a dinuclearoxovanadium(V) complexes by mixing of N'-(2-hydroxy-5-methylbenzylidene)–4-methylbenzohydrazide and $[VO(acac)_2]$ in methanol and Complex reacted with 3-hydroxy-2-methyl-4-pyrone to produce a mononuclear VO(V) complex. By using X-ray single crystal determination, IR, UV, and 1H NMR spectroscopy, the hydrazone and both complexes were characterized. In both complexes, the V atoms are coordinated octahedrally. According to the biological test, the complexes exhibit good antibacterial activity against the strains of *E. coli, B. subtilis, P. aeroginosa*, and *S. aureus bacteria.*

*Sharma, N., et al*[62] synthesized the oxidovanadium(IV) complex in methanol (MeOH) + tetrahydrofuran. The structure of the complexes is [VO(acac)(SHA)] where acac = acetylacetone, SHA = salicylhydroxamic acid and complexes is characterized , FTIR spectra showed that the oxygen atoms hydroxamic and carbonyl form a bond with the salicylhydroxamate ion. Using the conventional conjugate-gradient method, DFT/SIESTA was able to obtain an optimized deformed square-pyramidal geometry around vanadium. The HOMO–LUMO energy values are used to compute the molecular characteristics, such as the ionization potential, , chemical potential (μ), electronegativity (χ), and electrophilicity index (ω). According to the MIC technique, the complex's antibacterial

activity against bacterial strains like *S. aureus, S.epidermidis,* and *K. pneumonia* has demonstrated its capacity as a growth-inhibiting agent.

*Sharma, B.P., et al*[63]created novel mononuclear oxovanadium(IV) complexes. The complexes are examined using various spectroscopic techniques, conductivity measurement, FTIR, UV-Vis, and EPR. The analytical data has allowed for a thorough characterization of the complexes. The antibacterial sensitivity of the ligand and its metal complexes against bacterial pathogens investigated in vitro. *Muzaddadi, I.U., et al*[64]prepared the Oxidovanadium meso-tetrakis(3,4,5-trimethoxyphenyl) porphyrin complex. Cyclic voltammetry, UV-visible spectrophotometer, EPR, and NMR have all been used to characterize the complex. Analysis has been done on DNA binding and antibacterial analysis using a complex. The CV findings validate the complex-DNA interaction in the DNA-binding investigation. Furthermore, the complex increased ability to kill bacteria is evidence that the metal ions chelation with the porphyrin ligand makes it more lipophilic.

## 3.9 Antifungal Activity

*Sharma S et al*[65]consolidated a series of novel oxidovanadium(IV) complexes, denoted as $[VO(4\text{-}NO_2C_6H_4CH=CHCONHO)_2]$, $[VO(4\text{-}NO_2C_6H_4CH=CHCONHO)_2(2\text{–}CNC_5H_4N)]$, and $[VO(4\text{-}NO_2C_6H_4CH=CHCONHO)_2(4\text{-}CNC_6H_4NH_2)]$, and analyzed through a variety of analytical methods, including elemental analysis, magnetic susceptibility, molar conductivity, and, EPR, and mass spectrometry. By using the minimum inhibitory concentration method, the biological activity has been investigated against a variety of pathogenic bacteria, including *Salmonella paratyphi, Salmonella typhi,, Bruchypsectrafulva* and *Fusariumoxysporum.*The antifungal activity of compounds containing vanadium oxalate $\{(CH_6N_3)_2[VO(C_2O_4)_2]\}_n$ and $(C_7H_{11}N_2)_2[VO(C_2O_4)_2(H_2O)]\cdot 2H_2O$ against *Penicilliumitalicum* and *Penicilliumexpansum* has been studied by *Essghaier B et al*[66].

One of the several complexes of Oxovanadium(IV) has been created with substituted heterocyclic amine including 3-aminopyridine, 4-cyanopyridine, 2-aminopyridine, 4-aminopyridine by *Kapoor, S., et al* [67].These were described using a variety of physico-chemical criteria, including elemental analysis, electronic spectrum investigations, molar conductance measurements, magnetic moments, and IR spectra. For their biological activity against the pathogenic fungus, these complexes were evaluated. Antifungal action indicated by Sclerotium-rolfsii.

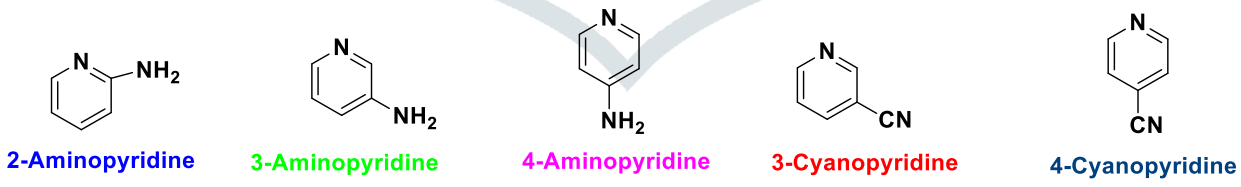
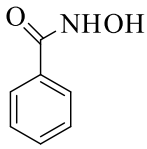
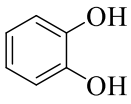



**Figure- 4 Substituted heterocyclic amines used during Oxovanadium(IV) complexes synthesis**

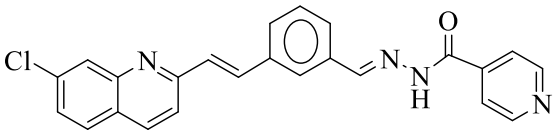
*Sinha, A. et al*[68] synthesized a set of new Cu(II) and V(V) complexes, including [VO(Quibal-INH) (cat)], $[VO_2$(Quibal-INH)], [VO(Quibal-INH) (bha)], and [Cu(Quibal-INH)2] among them Quibal-INH (L), an ON donor Schiff base ligand, as the main ligand. Analytical methods including $^{51}V$ NMR, ATR-IR, EPR, $^{1}H$ NMR, and UV-Vis were used to characterize the synthesized compounds. Ligand (L) and compound [VO(Quibal-INH) (cat)] showed a moderate level of growth inhibition against the fungus species *Candida albicans* and *Cryptococcus neoformans*.(**Complexes and ligands in Figure 5**)



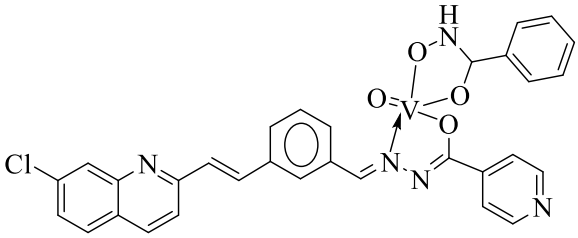
Benzohydroxamic acid (bha)



Catechol (cat)



Quibal-INH



[VO(Quibal-INH) (bha)]

**Figure- 5** Ligands for respective Cu(II) and V(V) complexes

*Maurya, M.R., et al*[69] synthesized complexes $[V^{IV}O(acac)_2]$ reacts with ligands derived from 2-(1-phenylhydrazinyl)pyridine and salicylaldehyde, 3-methoxysalicylaldehyde, 5-bromosalicylaldehyde in MeOH. Spectroscopic and single-crystal X-ray investigations verified the structures of the complexes. The antifungal and antiproliferative properties of these complexes were also assessed. *Candida albicans* and *Candida tropicalis* planktonic cells are effectively treated by these complexes at various MIC value. *Gayakwad, S.V., et al*[70]created synthetic mixed ligand complexes of V(IV) by reacting diazo ligands at room temperature with $VO(acac)_2$. IR and $^1H$ NMR spectra and particle XRD analysis are used to characterize all of the synthesized complexes. The produced complexes' antibacterial and antifungal properties against *U. maydis, A. flavus, A. niger,* and *S. rolfsii*, as well as against bacterial pathogens like *B. subtilis, P. aeruginosa, V. harveyi, and V. parahaemolyticus*, have been verified. The compounds anticancer, *in vitro* antidiabetic, and antioxidant properties have also been investigated.

## 3.10 Photocatalytic Activity

*Das Baishnab, S., et al.* [71] Two dioxidovanadium (V) complexes with a tridentate O, N, and O donor Schiff base ligand, salicylaldehyde–isonicotinoylhydrazone ($H_2L$), have been synthesised: $[VO_2LH]$ and $[\{VO_2L\}K(H2O)3]$. Elemental studies, FT-IR, UV-visible, and 1H NMR spectroscopy were used to structurally characterise the synthesised compounds. Under visible light, the complexes exhibit photocatalytic activity in the destruction of harmful cationic and anionic dyes, including brilliant blue, Congo red, methyl orange, xylenol orange, methylene blue, and rhodamine B in an aqueous media. *Jose, J.,et al.*[72] Vanadium complex anchored reduced graphene oxide (rGO-VO) was effectively produced by coordination interaction with trimethoxy silyl propanamine connected to phenyl azo salicylaldehyde**.** The synthesis of rGO-VO was verified by examining its physicochemical and microscopic characteristics using several analytical methods, including Fourier transform infrared spectroscopy, XRD, XPS, Raman spectroscopy, scanning electron microscopy, and transmission electron microscopy. According to photocatalytic experiments of anchored rGO-VO and $VO(acac)_2$ toward MB dye, anchored rGO-VO deteriorated more quickly than $VO(acac)_2$ when exposed to visible light-induced MB.

## 4. Conclusion

This review article focuses on a select few examples of the biological activity of vanadium(V) compounds. Vanadium coordination compounds are particularly promising, having attracted significant research interest due to their involvement in biological activity and potential medicinal applications. The review highlights that mixed-ligand complex of vanadium exhibit biological activity against bacteria and fungi. Additionally, these complexes hold promise for medicinal applications.

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## Declaration of competing interest

The authors state that none of their known financial conflicts or interpersonal connections could have influenced the work that was published in this paper.

## The Statement of compliance with standards of research involving humans and animals

This review article does not contain any studies involving human participants and animals performed by any of the authors.

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## Abbreviations

1, 10-phen = 1, 10-phenanthroline; FTIR = Fourier transform infrared spectroscopy; DTG = Differential thermogavemetric analysis; MIC= minimum inhibitory concentration; $^{51}$V-NMR=Vanadium-51 nuclear magnetic resonance; ATCC= American Type Culture Collection; bpy = 2,2´-bipyridine; sal-gly = N-salicylidene-glycine; sal-pheala = N-salicylidene-DL-β-phenylalanine; sal-leu = N-salicylidene-leucine; DPPH = 2,2-diphenyl-1-picrylhydrazyle; sal-met = N-salicylidene-DL-methionine; IR=Infra-Red; UV=Ultraviolet; V=Vanadium; VO=Oxo-vanadium; SOD= superoxide dismutase; FA=folic acid; AA=amino acids; FE-SEM= field emission scanning electron microscopy; sal-ala= N-salicylidene-β-alanine; DFX = Deferasirox; TG = Thermogravimetric; DMSO = Dimethyl sulfoxide; MCF= Michigan Cancer Foundation;