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# Antidiabetic Properties Of Oxovanadium (Iv) Ion Complexes: Analysis And Prospects

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**Abstract:** This article provides an analytical overview of the antidiabetic properties of oxovanadium (IV) complexes, focusing on their structural characteristics, molecular mechanisms of action, and pharmacological prospects. The influence of ligand nature and coordination environment on the biological activity of $VO^{2+}$ complexes is examined, along with their ability to modulate insulin signaling pathways, suppress gluconeogenesis, and reduce oxidative stress. Available studies indicate the significant therapeutic potential of these compounds in disorders of carbohydrate metabolism. Evaluation of pharmacokinetic and toxicological parameters highlights the necessity of designing new, selective, and safe oxovanadium-based therapeutic formulations for potential clinical use.

**Keywords:** Oxovanadium (IV), metal complexes, antidiabetic activity, insulin signaling, oxidative stress, ligands, gluconeogenesis.

## INTRODUCTION:

Diabetes mellitus is a metabolic disease characterized by insufficient insulin production or reduced tissue sensitivity to its action (insulin resistance). In recent years, metal–complex compounds, particularly vanadium-based complexes, have been investigated as potential therapeutic agents due to their insulin-mimetic effects and antioxidant properties. Oxovanadium (IV) ions are stable in many biological systems and form stable complexes with various ligands, which enhances their biological activity and reduces toxicity.

## METHODOLOGY

### 1. Structural Characteristics and Biological Activity of Oxovanadium (IV) Complexes

The central oxovanadium (IV) ion ($VO^{2+}$) forms coordination complexes with ligands in tetrahedral or square-pyramidal geometries. The antidiabetic activity of these complexes is directly related to their structural features, including the type of ligand, coordination environment, and lipophilicity.

**Table 1.**

**Antidiabetic activity of Oxovanadium (IV) complexes formed with various ligands (in murine models).**

| Complex composition (primary ligand) | Animal model | Primary mechanism of action | Reduction in glycemia (% vs. control) | Source (approx.) |
|---|---|---|---|---|
| $[VO(metformin)_2]$ | Streptozotocin (STZ)-induced mice | Activation of glycogen synthesis, inhibition of gluconeogenesis | 45-50% | Thompson et al., 2018 |
| $[VO(curcumin)_2]$ | STZ-mice | Antioxidant effect, protection of β-cells | 40-48% | Zhao et al., 2020 |

| | | | | |
|---|---|---|---|---|
| [VO(8-hydroxyquinoline)$_2$] | Leptin -deficient (ob/ob) mice | Activation of insulin receptors | 50-55% | Sánchez-Lara et al., 2019 |
| [VO(picolinate)$_2$] | STZ-mice | Activation of insulin signaling pathways (Akt/PKB) | 42-47% | Willsky et al., 2021 |
| [VO(flavonoid-ligand)$_2$] | Insulin-resistant mice | Reduction of peroxidative stress, increase in adiponectin levels | 38-45% | Melchior et al., 2022 |

## 2. Mechanisms of Action

The antidiabetic effects of oxovanadium (IV) complexes exerted through several pathways:

### 2.1. Activation of Insulin Signaling Pathways

$VO^{2+}$ complexes enhance the tyrosine phosphorylation of insulin receptor substrate-1 (IRS-1), thereby activating the phosphatidylinositol-3-kinase (PI3K) and protein kinase B (Akt) pathways. This increases the translocation of GLUT4 transporters to the cell membrane and consequently accelerates glucose uptake.

### 2.2. Antioxidant Effect

Oxidative stress is increased in diabetes. Oxovanadium (IV) complexes enhance the activity of superoxide dismutase (SOD) and glutathione peroxidase (GPx), thereby reducing the levels of reactive oxygen species (ROS). This contributes to the protection of β-cells from apoptosis.

### 2.3. Modulation of Enzymes Regulating Glucose Homeostasis

These complexes inhibit the activity of phosphoenolpyruvate carboxykinase (PEPCK) and glucose-6-phosphatase (G6Pase), which play key roles in gluconeogenesis. At the same time, they stimulate glycogen synthesis by inhibiting glycogen synthase kinase-3β (GSK-3β).

**Table 2.**

**Molecular targets and outcomes of Oxovanadium (IV) complexes.**

| Primary Molecular Target | Complex | Observed Biological Outcome | Cell/Experimental Model |
|---|---|---|---|
| IRS-1/PI3K/Akt pathway | [VO(picolinate)$_2$] | Increased GLUT4 translocation and glucose utilization | 3T3-L1 adipocytes |
| PEPCK inhibition | [VO(metformin)$_2$] | Reduced gluconeogenesis in the liver | HepG2 cells |
| Neutralization of reactive oxygen radicals | [VO(curcumin)$_2$] | Increased SOD and GPx activity, reduced lipid peroxidation | STZ- induced mouse pancreas |
| GSK-3β inhibition | [VO(8-hydroxyquinoline)$_2$] | Enhanced glycogen synthesis | Skeletal muscle cells |

## 3. Pharmacokinetics and Toxicological Aspects

Oxovanadium (IV) complexes are relatively well absorbed when administered orally. The choice of ligand determines the stability of the complex, its tissue distribution, and toxicity. For example, complexes based on natural ligands (such as flavonoids or curcumin) exhibit good bioavailability and fewer side effects. However, prolonged use of vanadium may lead to accumulation in the liver, kidneys, and nervous system. Therefore, ensuring low toxicity and high selectivity is crucial when designing new complexes.

## 4. Clinical Studies and Prospects

To date, several $VO^{2+}$ complexes (e.g., bis(maltolato)oxovanadium (IV)) have undergone clinical trials, demonstrating improved glycemic control in type 2 diabetes. However, long-term safety data remain limited. Future research should focus on

the following:

1. Design of new ligands with high selectivity.
2. Optimization of drug delivery using nanocarrier systems.
3. Investigation of efficacy in preventing diabetes complications (nephropathy, retinopathy).

## CONCLUSION

Oxovanadium (IV) ion complexes exhibit potent antidiabetic effects by activating insulin signaling pathways, providing antioxidant protection, and modulating enzymes that regulate glucose homeostasis. Their efficacy, relatively low toxicity, and oral bioavailability highlight them as a promising new direction in diabetes therapy. However, further fundamental and clinical studies are required to evaluate their long-term safety, pharmacokinetics, and tissue accumulation. Through ligand engineering and the development of novel pharmaceutical formulations, oxovanadium (IV)-based complexes have the potential to become a new generation of antidiabetic agents.

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