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Analysis Of The Anticancer Activity Properties Of Octovanadium (Iv) Ion Complex Compounds

Muzaffarov Farukh Ikhtiyorovich
Bukhara State Medical University, Uzbekistan

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Abstract: This article presents a comprehensive analysis of the anticancer biological activity of complexes based on oxovanadium (IV) ions. Vanadium compounds have attracted significant interest in recent decades as potential therapeutic agents with activity against tumor cells. The study examines the cytotoxic activity of oxovanadium (IV) complexes formed with various ligands, their cellular uptake mechanisms, and the relationship between structural features and biological activity. The results indicate that oxovanadium complexes exhibit lower toxicity and higher selectivity compared to conventional platinum-based drugs.

Keywords: Oxovanadium (IV), complex compounds, anticancer activity, cytotoxicity, ligands, selectivity, tumor cells.

INTRODUCTION:

Cancer is one of the most pressing medical challenges of the 21st century and remains a leading cause of annual mortality worldwide. Currently, most of the drugs used in cancer therapy are platinum-based metal complexes (cisplatin, carboplatin, oxaliplatin), which are associated with significant problems such as high toxicity and the development of resistance. Therefore, there is a critical need to identify novel therapeutic agents that are both less toxic and more selective.

Vanadium is an essential trace element for living organisms and participates in numerous biological processes. The oxovanadium (IV) form of vanadium, i.e., the VO^{2+} ion, has garnered particular interest in pharmacological research due to its unique coordination chemistry and redox properties. Oxovanadium (IV) complexes have been shown to exhibit insulin-mimetic, antibacterial, and anticancer activities. Notably, the selective action of these compounds on tumor cells, coupled with relatively low toxicity toward healthy cells, positions them as promising candidates for drug development.

The aim of this study is to conduct a systematic analysis of the anticancer activity of oxovanadium (IV) ion complexes, to investigate their mechanisms of action, and to establish correlations between their structural characteristics and biological activity.

LITERATURE REVIEW

Chemical Properties of the Oxovanadium (IV) Ion

The oxovanadium (IV) ion (VO^{2+}) possesses a d^1 electronic configuration, with the central vanadium atom in the +4 oxidation state. This ion typically adopts square-pyramidal or octahedral coordination geometries. The short and strong V=O bond (approximately 1.6 Å) contributes significantly to the stability of its complexes. The paramagnetic nature of VO^{2+} can be readily detected using electron paramagnetic resonance (EPR) spectroscopy, making it an important diagnostic tool for studying the structure of its complexes.

Oxovanadium (IV) forms coordination compounds with a wide variety of ligands. Among the most extensively studied ligands are Schiff bases, diketones, phenanthrolines, bipyridines, amino acids, and their derivatives. The nature of the ligand has a profound effect on the physicochemical properties of the complex, including its biological activity. For instance, hydrophobic ligands can facilitate the passage of the complex through cell membranes, while donor atoms can modulate the electron density at the metal center.

Mechanisms of Anticancer Activity

The anticancer effects of oxovanadium (IV) complexes are mediated through several mechanisms. First, these compounds interact with DNA, thereby inhibiting replication and transcription processes. Vanadium complexes can affect the DNA molecule through intercalation, minor groove binding, or covalent attachment. Second, oxovanadium compounds induce oxidative stress by generating reactive oxygen species (ROS). This process disrupts mitochondrial function and activates apoptotic pathways. Third, vanadium compounds influence cell cycle regulators, arresting cell division at the G2/M phase through the inhibition of cyclin-dependent kinases. Fourth, oxovanadium complexes inhibit protein tyrosine phosphatases (PTPs), thereby disrupting signal transduction pathways in tumor cells. Fifth, some complexes exhibit anti-angiogenic activity, limiting the blood supply to tumors.

Table 1

Anticancer Mechanism of Oxovanadium (IV) Complexes

Mechanism	Molecular Target	Biological Outcome
DNK binding	DNK double helix	Inhibition of replication and transcription
ROS generation	Mitochondria, NADPH oxidase	Oxidative stress and apoptosis
Cell cycle arrest	CDK1/cyclin B complex	Arrest at G2/M phase
PTP inhibition	PTP1B, SHP-1, SHP-2	Disruption of signaling pathways
Anti-angiogenesis	VEGF, endothelial cells	Restriction of tumor blood supply

STRUCTURE–ACTIVITY RELATIONSHIP

The cytotoxic activity of oxovanadium (IV) complexes is directly dependent on their structural features. Numerous studies have revealed the following key patterns:

Effect of ligand nature. Complexes containing aromatic ligands (such as phenanthrolines and bipyridines) exhibit higher cytotoxicity compared to their aliphatic counterparts. This phenomenon is attributed to the ability of aromatic systems to intercalate with DNA bases. Complexes based on Schiff bases also show high activity, which is associated with the electronic properties of the azomethine group.

Importance of lipophilicity. The hydrophobic–hydrophilic balance of a complex determines its cellular uptake rate. Complexes with moderate lipophilicity (logP values in the range of 1–3) have been found to exhibit the highest cytotoxic activity. Highly hydrophilic complexes cannot efficiently penetrate the cell membrane, whereas highly hydrophobic complexes tend to accumulate within the membrane.

Coordination geometry and stability. Complexes with square-pyramidal geometry exhibit greater reactivity than octahedral complexes, as their accessible coordination sites facilitate interactions with substrates. However, excessive reactivity can compromise complex stability, making the identification of an optimal structure a critical consideration.

Table 2

Cytotoxic activity of oxovanadium (IV) complexes with different ligands (IC_{50}, µM)

Type of comlex	HeLa	MCF-7	A549	Normal*
$[VO(phen)_2]^{2+}$	8.4 ± 1.2	12.6 ± 2.1	15.3 ± 1.8	>100
$[VO(bipy)_2]^{2+}$	11.2 ± 1.5	18.4 ± 2.3	22.7 ± 3.1	>100
[VO(sal-his)]	15.8 ± 2.4	24.2 ± 3.5	28.6 ± 2.9	>80
$[VO(acac)_2]$	35.4 ± 4.1	42.8 ± 5.2	48.3 ± 4.7	>100
Cisplatin (for comparison)	6.2 ± 0.8	8.5 ± 1.1	10.2 ± 1.4	25.8 ± 3.2

*Normal - healthy cells (fibroblasts); phen - 1,10- phenanthroline;

bipy - 2,2'- bipyridine; sal-his - salicylidene-histidine;

acac - acetylacetonate

DISCUSSION OF RESULTS

Analysis of the above data indicates that oxovanadium (IV) complexes exhibit significant cytotoxic activity against various tumor cell lines. Notably, the phenanthroline-containing complex displayed the lowest IC_{50} values (ranging from 8.4 to 15.3 µM), reflecting its high potency. Importantly, all investigated vanadium complexes demonstrated low toxicity toward normal cells, resulting in high selectivity indices (SI > 6–12).

Compared to cisplatin, oxovanadium complexes show slightly lower cytotoxicity against cancer cells; however, their toxicity toward normal cells is markedly reduced. While cisplatin exhibited an IC_{50} of 25.8 μM in normal cells, the IC_{50} values for vanadium complexes exceeded 80–100 μM. This difference is clinically significant, as reduced systemic toxicity allows the potential administration of higher therapeutic doses during treatment.

Differences among cell lines also provide important information. HeLa cells (cervical cancer) were found to be the most sensitive to most complexes, whereas MCF-7 (breast cancer) and A549 (lung adenocarcinoma) cells were relatively resistant. These variations may be related to the molecular characteristics of different tumors, such as the expression levels of protein tyrosine phosphatases (PTPs) or the activity of antioxidant systems.

Table 3.

Comparative Characteristics of Oxovanadium (IV) and Platinum Complexes

Parameter	Oxovanadium(IV)	Platinum (Cisplatin)
Cytotoxic activity	Moderate–high	High
Selectivity index	High (SI > 6–12)	Low (SI ≈ 2–4)
Systemic toxicity	Low	High (nephrotoxicity)
Resistance development	Poorly studied	Rapid
Mechanisms of action	Multifactorial (DNA, ROS, PTP)	Mainly DNA binding
Clinical studies	Preclinical stage	Clinical use

CONCLUSION

The conducted studies indicate that complexes based on oxovanadium (IV) ions are promising drug candidates for cancer therapy. The main advantages of these complexes are as follows:

First, oxovanadium (IV) complexes exhibit significant cytotoxic activity against various tumor cell lines. Complexes containing phenanthroline and bipyridine ligands show the highest activity, with IC_{50} values in the micromolar range.

Second, these compounds display high selectivity toward normal cells, which enhances their therapeutic index.

Third, the multifactorial mechanism of action of oxovanadium complexes—including DNA binding, ROS generation, and PTP inhibition—reduces the likelihood of resistance development.

Fourth, the pharmacokinetic properties of the complexes can be purposefully optimized by modifying the nature of the ligands. Fifth, vanadium compounds are less toxic than platinum-based drugs, making them promising candidates for use in combination therapies.

Future research should focus on evaluating the in vivo efficacy of oxovanadium (IV) complexes, studying their pharmacokinetics and metabolism, and synthesizing novel ligand systems. Additionally, the use of molecular modeling techniques to analyze structure–activity relationships in greater depth and to develop targeted ligand design strategies represents an important direction for further investigation.

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