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# Polyoxovanadates Contribution to Pharmacological, Antimicrobial and Toxicological Actions of Vanadium †

**Gil Fraqueza [1,2] and Manuel Aureliano [1,3,*]**

[1] Instituto Superior de Engenharia, Universidade do Algarve, 8005-139 Faro, Portugal; gfraque@ualg.pt
[2] Faculdade de Ciências e Tecnologia (FCT), University of Algarve, 8005-139 Faro, Portugal
[3] Centro de Ciências do Mar (CCMar), University of Algarve, 8005-139 Faro, Portugal
* Correspondence: maalves@ualg.pt
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**Abstract:** Studies of the pharmacological action of vanadium compounds have shown that vanadium has been arousing interest as a potential candidate for therapeutic applications. Polyoxovanadates (POVs) emerge from polyoxometalatates (POMs) and are responsible for an increase in the number of vanadium studies on multidirectional biological activity in view of their application in biomedicine. In fact, increasing research studies have shown POVs' anti-bacterial, anti-fungal, anti-parasitic, anti-viral, anti-cancer as well as anti-diabetic activities. Herein, we highlight decavanadate and decavanadate compounds, perhaps the most studied POVs in biology, strengthening the potential use of such metallodrugs in the future. Thus, vanadium compounds, including POVs, show a great potential in the treatment of many types of diseases.

**Keywords:** polyoxometalates; polyoxovanadates; decavanadate; antibacterial agents; drug discovery; metal-based drugs



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## 1. Introduction

Vanadium (V) is an element with a wide range of effects on the mammalian organism [1,2]. The ability of this metal to form polyoxovanadates (POVs) and organometallic compounds has contributed to the increase in the number of studies on multidirectional biological activity in view of their application in medicine [3–7]. Vanadium compounds receive a great deal of attention from chemists, biologists, biochemists, toxicologists, and pharmacologists. The biological activity of compounds containing this element has resulted in many investigations of many organic vanadium complexes and its inorganic compounds in terms of their potential use in the treatment of certain diseases in humans. Studies carried out so far on vanadium compounds have shown that the bioactive complexes/compounds of this metal can be therapeutically active at low concentrations [1,3]. The structures of several vanadium complexes including POVs, showing several biological and biomedical activities, were described elsewhere [3,5–8].

## 2. Vanadium in Biology, Toxicology and Pharmacology

Vanadium is essential in trace amounts (0.05 μM) and toxic in excess (>10 μM) [1,2]. Vanadium at the highest oxidation state (+5) is the most toxic vanadium form, and vanadium pentoxide ($V_2O_5$) is the most toxic form of this metal [1]. The redox properties of vanadium are a determinant of its pharmacological effects because it can inhibit or stimulate enzymes. Similarly, due to the ability of vanadium to adopt a variety of coordination geometries, the rich structural chemistry of POVs might be responsible for the increased interest in their biology and biomedical applications [5–7]. Many studies have revealed, at the molecular level, the interaction of vanadate, POVs and organometallic compounds containing vanadium with enzymes and have revealed them to have a toxic

activity on these enzymes, in particular by inhibiting their activity. The enzymes most studied are phosphatases, PTPases, kinases, glucose-6-phosphate dehydrogenase, triphosphate diphosphohydrolases, phosphodiesterases, phosphoglucomutases and ATPases [5,7,9].

The inhibitory effects of vanadium compounds are observed in ion pumps such as $Na^+/K^+$ ATPase, $H^+/K^+$ ATPase and $Ca^{2+}$-ATPase, and interestingly, the isopolyoxovanadate decavanadate $[V_{10}O_{28}]^{6-}$ is a more potent $Ca^{2+}$-ATPase inhibitor than monomeric vanadate [10–12]. A recent study with several POVs, namely $[V_{10}O_{28}]^{6-}$ ($V_{10}$), $[H_6V_{14}O_{38}(PO_4)]^{5-}$ ($V_{14}$), $[V_{15}O_{36}Cl]^{6-}$ ($V_{15}$) and $[V_{18}O_{42}I]^{7-}$ ($V_{18}$), demonstrated their inhibitory effect on three major multidrug resistance-linked ABC transporters: P-glycoprotein (P-gp), ABCG2 and MRP1, opening the door to a potential strategy for overcoming multidrug resistance via the use of inhibitors of ABC drug transporters [13]. In fact, POVs have been referred to as polyoxometalates with several biological activities [5,7,9] and constitute a rapidly growing field [5–7,9]. Moreover, POVs were used in the degradation of emerging pollutants, indicating that the future is bright in environmental and biomedical research [7]. Examples of several POV structures can be found elsewhere [5]. The isopolyoxovanadate decavanadate ($V_{10}$) is perhaps the most studied in biology, playing many important roles in fundamental processes [5–7,9,11,14,15].

The mechanisms of toxicity of POVs require further experimental work, as they have not yet been fully elucidated. However, POVs induce many biological effects by affecting several processes, such as oxidative stress, lipoperoxidation, apoptosis, cell cycle arrest, interference with ions transport systems, inhibition of mRNA synthesis, cell morphology changes, changes in metabolic pathways, phosphorylase enzyme inhibition and cell signalling, inhibition of viral mRNA polymerase, inhibition of virus binding to the host cell, and penetration and interaction with virus protein cages, among others [5–7]. The biological activity of compounds containing this element has resulted in many investigations on many organic vanadium complexes as well as on its inorganic compounds in terms of their potential use in the treatment of certain diseases in humans. In fact, many research studies have described, among others, anti-bacterial, anti-fungal, anti-parasitic, anti-viral anti-cancer, anti-diabetic, and anti-hypercholesterolemic activities and cardioprotective, neuroprotective, and anti-obesity effects resulting from vanadium compounds, complexes and/or POVs (Figure 1).

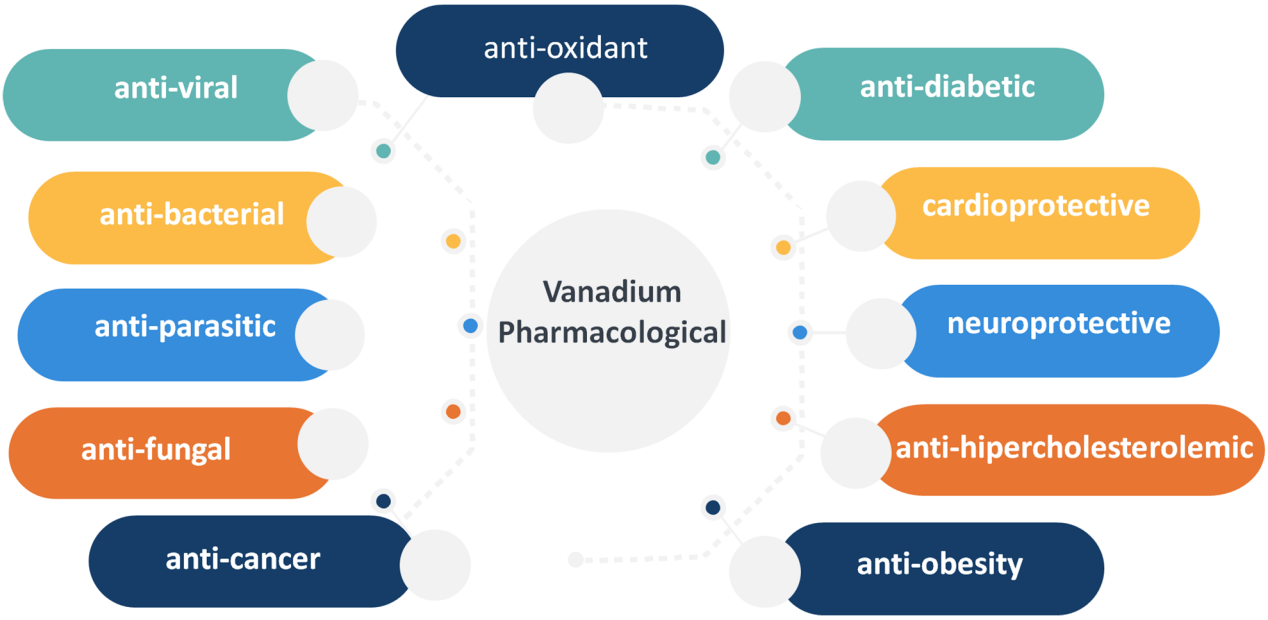


**Figure 1.** Pharmacological and/or biological activities of vanadium compounds including POVs.

## 3. POVs' Contribution to Antimicrobial Activities of Vanadium

As referred to above, vanadium compounds present antimicrobial activity. Several studies have demonstrated the pharmacological potential of vanadium compounds and/or POVs, showing that some compounds/complexes of this element can be effective against many microbial diseases, such as: (a) viruses, including dengue virus, influenza, HIV-1 virus and HIV-2 immunodeficiency virus, and severe acute respiratory syndrome (SARS) virus [16,17] responsible, respectively, for dengue fever, acute respiratory infection, acquired immune deficiency syndrome (AIDS) and SARS; (b) parasitic protozoan diseases caused by the genus *Trypanosoma* responsible for American trypanosomiasis and African trypanosomiasis, known as Chagas disease and sleeping sickness, respectively; protozoan parasites of the genera *Leishmania* and *Entamoeba* [17–23] responsible for the development of leishmaniasis and amoebiasis, respectively; (c) mycotoxicosis caused by the genera *Candida*, *Aspergillus*, *Trichophyton*, and *Microscopus* [24–26]; and (d) bacterial diseases caused by Gram-negative and Gram-positive bacteria [27–29], such as food poisoning, gastrointestinal disease, typhoid fever, respiratory infections, tuberculosis, pneumonia, strep throat and skin diseases.

Bacterial resistance to antibiotics has led researchers to find compounds with a potential antibacterial action and/or with the ability to reverse antibiotic resistance. Polyoxovanadates (POVs) and polyoxotungstates (POTs) are inorganic-based clusters that may fulfill this need. In fact, it was reported that polyoxometalates (POMs) showed the ability to disturb microorganisms that were either susceptible or resistant to antibiotics [5–7,15,29]. Moreover, some POTs present antiquorum sensing and anti-biofilm activities besides being potent antibacterial agents against *S. aureus* and exibiting antiviral activities against enteric viruses [30].

## 4. Conclusions

The biological activity of vanadium has demonstrated an essential role of this element. Vanadium compounds, including POVs, have been shown to regulate the activity of key enzymes involved in the phosphorylation and dephosphorylation of proteins, kinases, and phosphatases, taking part not only in carbohydrate and lipid metabolism but also in cell proliferation and differentiation.

POVs have made a relevant contribution to the increasing interest in the pharmacological action of vanadium compounds. Several studies have shown that vanadium has been arousing interest as a potential candidate for therapeutic applications. POVs present anti-bacterial, anti-fungal, anti-parasitic, anti-viral and anti-cancer activities, among others, which points to promising applications in a near future.

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