Open Access

SCHOLARENA

Journal of Molecular Biology and Biochemistry

RESEARCH ARTICLE

The Potency of Vanadium Compounds in Medicinal and Health Issues

Dieter Rehder*

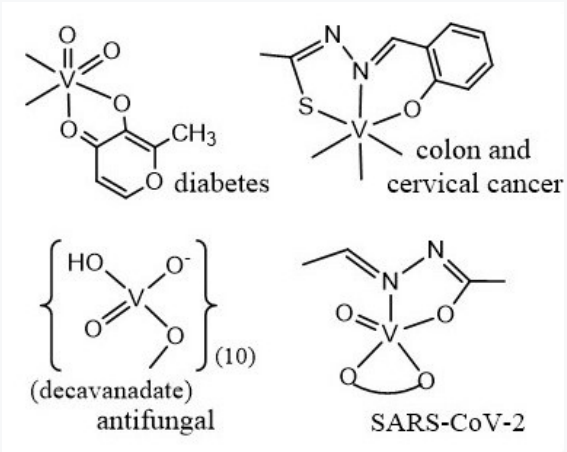
Chemistry Department, University of Hamburg, Germany

***Corresponding Author:** Dieter Rehder, Chemistry Department, University of Hamburg, Germany, E-mail: dieter.rehder@uni-hamburg.de

Citation: Dieter Rehder (2024) The Potency of Vanadium Compounds in Medicinal and Health Issues, J Mol Biol Biochem 3: 101

Abstract

The vanadate/phosphate antagonism is a significant issue when tracing back the impact of vanadium compounds (and their degradation products at physiological conditions) in health issues – i.e. the positive as well as potentially hazardous bearing on medicinally eminent functions. Contrasting phosphate, vanadate and its physiologically relevant vanadium-based precursor products (coordination compounds in particular) are subject to reduction (essentially to the oxidation state +IV and – less prominent – +III), and to the ability of the oxido cations (VO_2^+ and $VO^{3+/2+}$) and vanadate(s) (such as $H_2VO_4^-$) to coordinate to and to interact with physiologically relevant organics. Consequently, in the present compilation, the following aspects will be addressed: (i) the level of the phosphate/vanadate antagonism as well as their comparative and/or matchable behavior in the physiological broth, and (ii) the specific features of the oxidovanadium cations (and to a certain extent, of V^{3+} as well) in their function as (redox-active) coordination centers in potential medications, including redox inter-conversion, internal transformation, and accompanying physiological effects. The impact of vanadium coordination compounds in the (prospective) treatment of corona, microbial infections, diabetes and cancer will be addressed, with the more recent results being prioritized; see graphical abstract for a simplified overview.



Graphical Abstract

Keywords: Phosphate Antagonism; Vanadium Compounds; Organic Biochemistry

Vanadate and Phosphate

Figure 1 represents analogies as well as (essentially minor) disparities between tetrahedral vanadate and phosphate; Figure 2 is an example for the pentacoordinate environment of vanadium; pictured here for the binding to a serine residue in a phosphatase. At about neutral pH (pH = 7.4; i.e. at physiologically relevant conditions); the main species of free vanadate and phosphate are dihydrogenvanadate $H_2VO_4^-$ and monohydrogenphosphate HPO_4^{2-}; respectively; the pK_a values are 7.2 (for $H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$) and 7.8 (for $H_2VO_4^- \rightleftharpoons HVO_4^{2-} + H^+$). Below pH 3; (hydrated) VO_2^+ comes in; and at pH values above ca. 8; monohydrogenvanadate (HVO_4^{2-}) in equilibrium with $H_2VO_4^-$ incrementally dominates. The common mean concentration of vanadium in blood is around 200 nM [1a]. Further; mixed phosphate/vanadate species can form as shown in eq. (1). In contrast to phosphate; vanadate – with increasing pH – progressively oligomerizes to form; inter alia; tetravanadate $V_4O_{12}^{4-}$ and decavanadate $HV_{10}O_{28}^{5-}$ (in the presence of hydrogenperoxide; (physiologically labile) peroxidophosphates and -vanadates come in). In the pH region 1-11; there are up to nine different vanadate/phosphate species; at neutral pH; and in physiological media (0.15 M Na^+Cl^-); the ternary/quaternary systems H^+-$H_2VO_4^-$-phosphate/H_2O_2 dominate [1b].

$$H_2VO_4^- + H_2PO_4^- \rightarrow H_2VPO_7^{2-} + H_2O \quad (1)$$

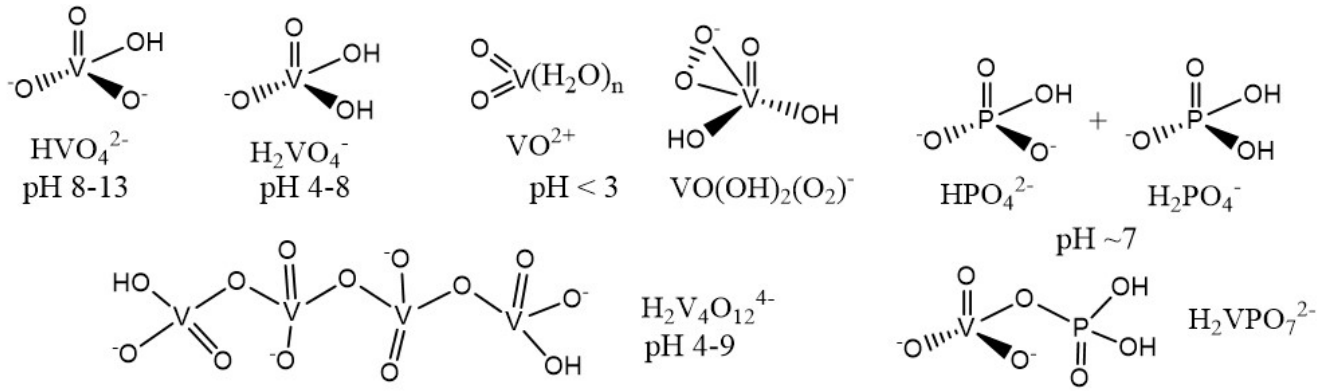


Figure 1: Vanadates; phosphates; and phosphovanadate [2] at about physiological pH. At acidic conditions (between pH 6 and 2.5); decavanadate $H_2V_{10}O_{28}^{4-}$ comes in

Along with these similarities between vanadate and phosphate there are also distinct differences; that at least partially result in adverse (and hence potentially toxic) effects. In particular; the transition metal vanadium (essentially in its cationic forms VO^{2+} and VO^{3+} present in natural systems; as well as in its anionic appearance; i.e. vanadates) tends to extend its coordination sphere via the formation of coordination compounds; chiefly with the coordination numbers 5 to 7; with (potential) ligands available in the physiological broth. As an example; the coordination of vanadate to alkaline phosphatase [3] (with a typical coordination environment close to a trigonal-bipyramidal structural arrangement [4]) is shown in Figure 2. The chemical as well as physiological affinity between vanadate(s) and phosphate(s) on the one hand; and their disparities in electronic structure on the other hand; are basic parameters for their related (and; in part; cooperative) as well as the clearly distinct physiological conduct (including – by trend – the potential toxicity of vanadate); and hence of their (feasible) therapeutic applications [5]. An overview on reported structures of vanadium protein complexes has been provided by Santos and Costa Pessoa [6a]. For a more recent example – the binding of redox-active hexavanadate to biotin binding proteins (such as avidin) – see [6b].

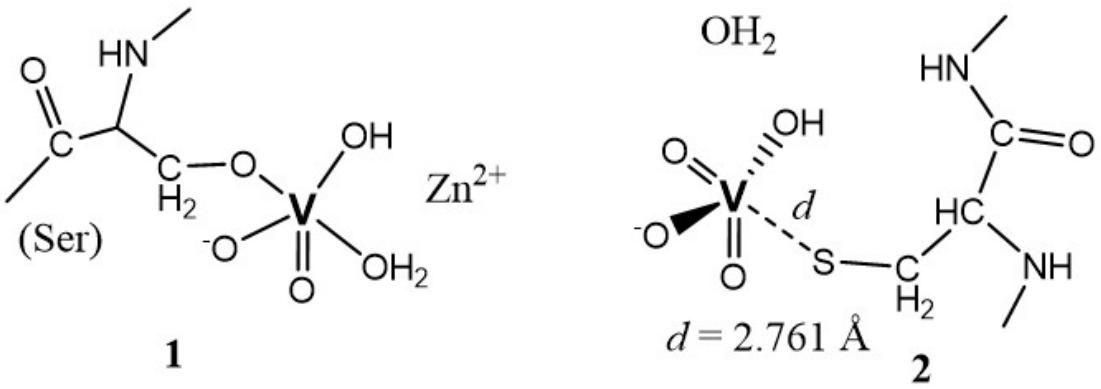


Figure 2: The coordination environment of vanadate bound to alkaline phosphatase (**1**; adapted from ref. [2a]) and tyrosine phosphatase (2; adapted from ref. [4a])

On a general basis; the (structural and commonly functional) similarities between vanadate and phosphate; as well as the distinct differences (in particular as far as the ability to form coordination compounds and the redox activity of vanadate and oxidovanadium are concerned); vanadate and phosphate can be considered to be in a widely managed competition in the physiological broth; see; e.g. ref. [7]. Examples for the potential toxicity of vanadium in general [8a]; and vanadium coordination compounds in particular; are the non-innocent oxidovanadium(V) Schiff base complexes with catecholate ligands; tested for their anticancer activity [7]; and the apoptosis induced in HeLa cancer cells [8b]. Divanadate (formed from orthovanadate) kills bacteria via cell wall destruction as a result of strong coordination to Ca^{2+} and Mg^{2+}; thus deactivating phosphatase and consequently cell wall synthesis [8c].

Chemico-Biological Interactions

A primary in-depth analysis of the interactions of vanadate with constituents of human blood goes back to the groups of Pettersson [9a] and Mukherjee [9b] about two decades ago. In many cases; the *active* component of the chemico-biological interaction of vanadium and its compounds appears to be non-complexed vanadium (i.e. vanadate as well as oxidovanadium(V) and -(IV)); suggesting that the role of the ligands is restricted to an efficient translocation of vanadate anions (or oxidovanadium cations) to the site of (medicinal) action. $H_2VO_4^-$ and VO^{2+} (as well as other cationic forms such as VO^{3+}; VO_2^+ and $V_2O_3^{4+}$ [10]) can pass the cell membrane via ion channels (in particular phosphate channels in the case of $H_2VO_4^-$); or by passive diffusion across the cell membrane [11]. Along with phosphate (see Figure 1) and carbonate (eqn. (2) [12]); free acid anions such as glycinate; lactate and citrate as well as (fragments of) proteins can function as "transporters" (commonly via the formation of coordination compounds) for vanadate and oxidovanadium cations in the blood stream and other body fluids – via coordinative and non-covalent (van der Waals) interactions [13]; examples for such proteins are transferrin and albumin. As in case of the (potential) interaction between vanadate and phosphate/carbonate; the cation VO^{2+} can intervene with other (divalent) cations (e.g. Mg^{2+} [14]) present in the body tissues.

$$H_2VO_4^- + HCO_3^- \rightarrow HVO_3CO_3^{2-} + H_2O \quad (2)$$

Vanadium complexes such as $[V^{IV}O(maltol)_2]$ and $[V^{V}O_2(maltol)_2]^-$ (in interchange with the V^{IV} varient) can form adducts with cytochrome-c; presumably (but not exclusively) via coordination to glutamate; and subject to interchange between the vanadium oxidation states IV and V [15]. In addition to simple inorganic vanadate and oligovanadates; (oxido)vanadium coordination compounds interact with various proteins; examples are phosphatases; kinases; and glutamases. The interplay takes place via; inter alia; hydrogen bonding; ion-pair [16a] van der Waals or covalent interaction [16b]; see Figure 3 for tetravanadate.

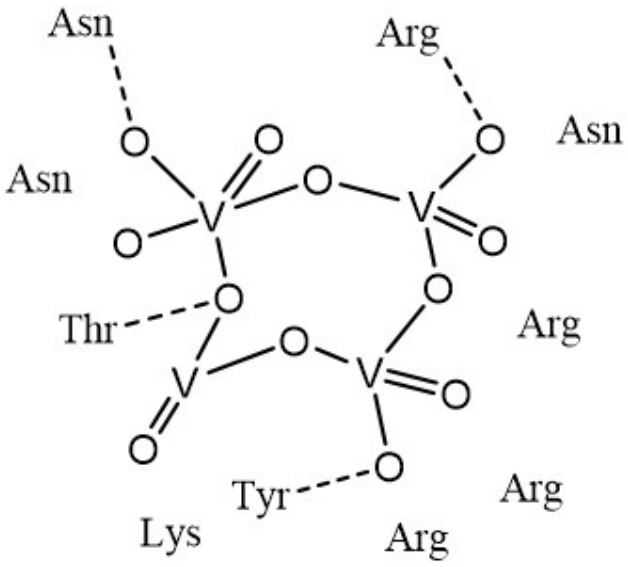


Figure 3: The hydrogen bonding interaction of tetravanadate incorporated into phosphoglycerate mutase (adapted from ref. [16b]).

Constitutional Vanadium Compounds

In this chapter; the potency; potentiality and side effects observed as vanadates (and/or vanadium coordination compounds) are being addressed; namely in the context of their potentiality in medicinal issues; i.e. their operative effectiveness in the therapy of diseases; including undesirable side effects. Since; at physiological conditions; there is an interplay between vanadium coordination compounds and vanadate; a clear differentiation commonly is not possible. The efficacy of vanadium (in the form of vanadate) in the treatment of ailments goes back to the year 1899; when diabetics were subjected to oral treatment with vanadate ($NaVO_3$ dissolved in water; i.e. $H_2VO_4^-$) [17a]). In the following layout; the focus will be directed towards the efficacy of vanadium-based (coordination) compounds; including (potential) side-effects; in the treatment of COVID-19; diabetes and cancer; for a recent review on therapeutic vanadium-based drugs in the treatment of cancer; see also ref. [18]. For an overview of medicinally active Schiff base complexes and oxidovanadium compounds effective in the treatment of cancer; fungal and bacterial infections and other biological (medicinal) activities see ref. [17b]. An artificial peroxidase with {V-Fe_2O_3} sites (4 in Figure 4) acts effectively against bacteria such as *Staphylococcus aureus*. *S. aureus*; a gram-positive bacterium; belongs to the normal flora of the skin and the mucous membrane; but eventually – when entering the body – is also pathogen; causing severe infections essentially of the skin. The compound catalyzes the oxidation (by H_2O_2) of Cl^- to HClO; which apparently is the active species [17c].

The potentiality of vanadium-based medications applied against the viral infection corona (COVID-19; SARS-CoV-2) – an affliction with an enlarged infectious risk for diabetic patients [19] – has recently been surveyed [20]. These effects of vanadium have been traced back to its antiviral; anti-inflammatory and antihyperglycemic impact; i.e. vanadium appears to alleviate risk factors for diabetes; presumably in the form of directly disposable vanadate; or the indirect delivery (i.e. via degradation of coordination compounds in body fluids). Decavanadate in particular has been shown to associate electrostatically with the positively charged segments of the receptor binding domain of the SARS-CoV-2 spike protein. Hence; it disrupts the protein binding to the host cell surface receptor and thus interferes with the entry of SARS-CoV-2 into the host cell; blocking off the docking of the virus to the cell surface receptor [21]. It should be noted; however; that decavanadate does also have cytotoxic effects.

Given the early evidence (1899) of the antidiabetic effect of vanadate [17a] and a first comprehensive; clinically supported study

of the respective potentiality of vanadium coordination compounds (an oxidovanadium-maltol complex) in 1995 [22]; it appears to be unreckoned that; so far; clinical application of (controllable) vanadium-based medications have not yet been broadly recognized or even generally established for the treatment of diabetes mellitus. The complex anion $[VO_2(maltol)_2]^-$(BMOV) (1 in Figure 4) is the predominant species present in the pH range 4.5 to 8.5; depending on the pH; species of composition $[VO_2(maltol)OH(H_2O)]^-$ and $[VO_2(maltol)(OH)_2]^{2-}$ also form. In any case; successive reduction to V^{IV} occurs [23]; with glutathione being the main reductant; and ATP (a strong binder for VO^{2+}) forming a mixed ligand (maltolate + ATP) VO^{2+} system; finally replacing maltolate via coordination of VO^{2+} to the terminal phosphate. In a similar manner; maltolate can be replaced by cysteinate (as a constituent of the tripeptide $_{\gamma}$-Glu-Cys-Gly) – though less efficiently than by phosphate [24]. Various binding sites and binding modes for the maltolato complexes and their hydrolysis and/or reduction products have been described; among these binding to the protein hen egg lysozyme. Binding occurs non-covalently ($[VO(malt)_2H_2O]$ and $[VO(malt)(H_2O)_3]^+$ and/or (commonly after hydrolytic removal of maltol) covalently ($[VO(H_2O)_{3-4}]^{2+}$) [25a]. Also; peptides can bind to the maltolato complex (2 in Figure 4). This includes simple peptides such as HisProAla [25b] and hemoglobin (Hb) [25c]. In the latter case; $[VO(maltol)_2\{His\}]$ (2 in Figure 4) is formed; i.e. coordination again occurs via the histidine-N and; in the case of Hb; additionally via Glu-O^- and/or Asp-O^- [25c].

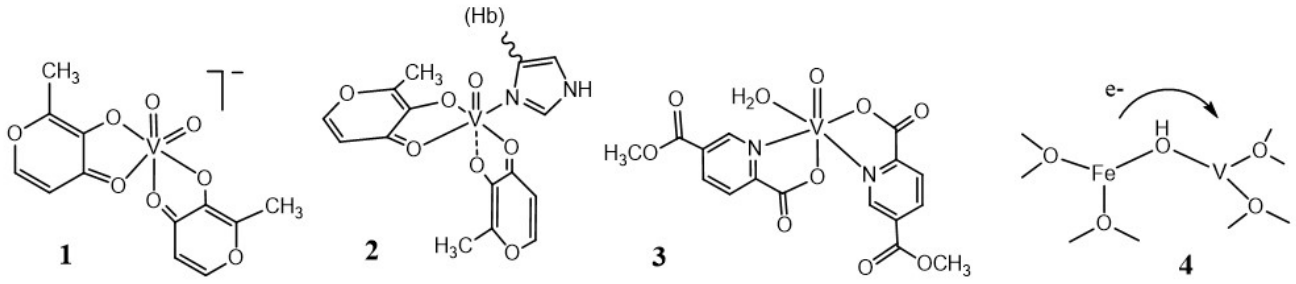


Figure 4: 1 to 3: A selection of vanadium compounds that have been shown to be effective in the treatment of diabetes: **1** $[VO_2(maltol)_2]^-$ (BMOV) [23]; 2 $[VO(maltol)_2His(peptide)]$ [25]; 3 $[VO(H_2O)(5MeOpic)_2]$ [26]. 4 The $\{V\text{-}Fe_2O_3\}$ sites in an artificial; antibacterial (*S. aureus*) peroxidase [17c]

A dioxido vanadium compound $[VO_2(ONN)]$ based on a trifunctional ONN ligand (L) (1 in Figure 5) has been shown to exhibit anticancer acivity [27]. The coordination compound 2 (Figure 5) and related complexes catalyzes the oxidation of benzyl alcohols by H_2O_2 to form the respective aldehydes. 2 exhibits antifungal and anti-proliferative activity; and is effective in the treatment of infections by; e.g.; fungal cells of *Candida* species [28]. The tetragonal-bipyramidal complex 3 in Figure 5 normalizes elevated glucose levels after oral gavage to Wistar rats; and consequently malfunctions accompanying diabetes [29]. The protein tyrosine phosphates PTP1B is involved in the insulin signaling pathway; and therefor related to diabetes and obesity. Inhibition of PTP1B phosphatase by docking of vanadate to the phosphatase triggers cellular glucose uptake and its successive degradation. V^{IV} (and also V^{III}) Schiff base complexes based on ONO donors; such as 4 in Figure 5; have been shown to be effective as insulin-mimetic compounds [30].

Antidiabetic (free fatty acid release from adipocytes) as well as anti-cancer (antiproliferative) effects have also been reported for the compound $[V^{IV}O(empp)_2(H_2O)]$ (empp = 1-methyl-2-ethyl-3-hydroxy-4(1H)pyridinone). The compound binds covalently to the *Asp* side-chain of lysozyme and non-covalently to Glu; Cys and Arg [31]; see 5 in Figure 5. Anti-diabetic compounds such as metformin-decavanadate have also been shown to exert therapeutic effects against skin cancer (human melanoma cells); likely via the inhibition of Ca^{2+}ATPase [32a]. The inhibition of melanoma cell development (IRG 39) has also been demonstrated for decavanadate [32b]. Damage of cancer-associated lysosomes - via production of reactive oxygen species - has also been demonstrated for compound 6 in Figure 5. 6 is marked by high hydrolytic stability; (i.e. retains its structure in solution); pronounced binding activity for CT-DNA; and exhibits marked potency against A549 cells [33]. For a recent overview of the ef-

ficiency of vanadium compounds in cancer therapeutics see ref. [34].

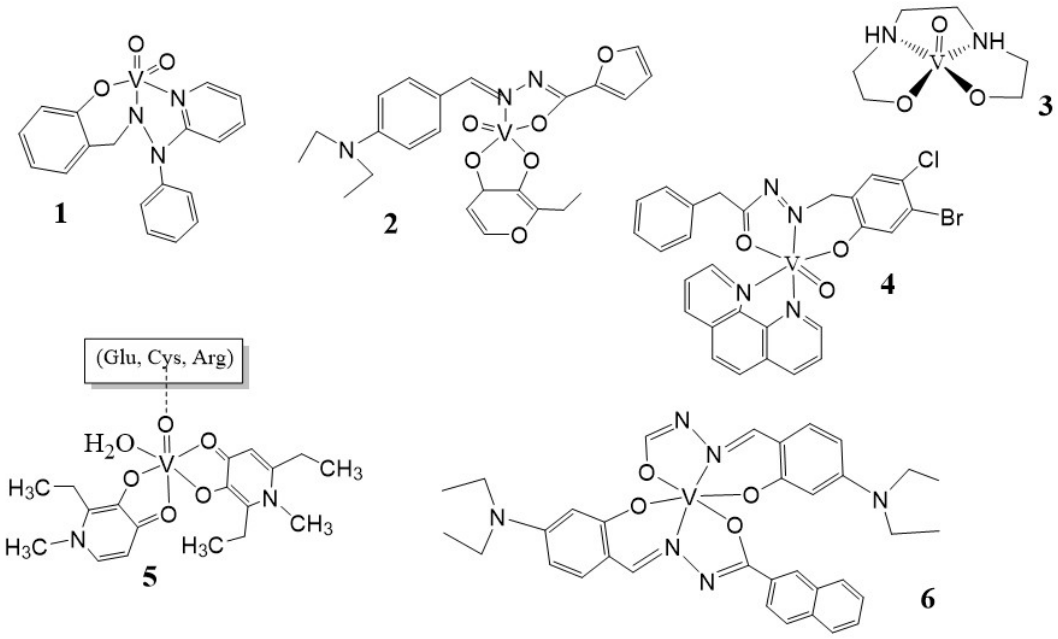


Figure 5: Vanadium coordination compounds that exhibit antifungal and antiproliferative (anticancer) activity. 1 $[V^{V}O_2(L^{1})]$ [27]; 2 $[V^{V}O_2(L^{2})]$ [28]; 3 $[V^{IV}O(L^{3})]$ [29]; 4 $[V^{IV}O(L^{4})]$ [30]; 5 Non-covalent interaction (hydrogen bonds; dashed line) between the coordination compound $[VO(empp)_2(H_2O)]$ and a lyosyme protein [31]; 6 $[V^{IV}(ONNO)_2]$ [33].

The treatment of patients with cancer (such as brain; lung and pancreas cancer) is often accompanied by bacterial infections with; e.g.; *Mycobacterium smegmatis* [35]. Growth inhibition of *M. smegmatis* is achieved with the uniquely stable; anti-cancerous Schiff base catecholato-vanadium coordination compound 2 (Figure 6); at a mean inhibitory concentration (dissolved in water + 10% DMSO) of 119 μM [36]. The water soluble dinuclear anionic complex 3 in Figure 6 is cytotoxic against the human hepatocellular carcinoma cell lines HepG2 [37]; the non-oxido complex 4 in Figure 6 undergoes partial oxidation at physiological conditions to form $[V^{V}L_2]^{+}$ and $[V^{V}O_2L]^{-}$. The compounds show non-covalent interaction as well as moderate binding affinity to bovine serum albumin; interaction takes place with tyrosine; lysine; arginine and threonine [38].

Antitumor activity against hepatocellular carcinoma has also been reported for the dimeric coordination compound $[V_2O_2(1;3\text{-pdta})]$ (pdta = propylenediamine) and the corresponding monomers [VO(ida)L]; where ida = iminodiacetate; and L = bipy or phen (5 in Figure 6) [39]. The compound blocks the synthesis of DNA and cell division; and thus induces apoptosis. The coordination compound 6 in Figure 5; containing a chromone Schiff base obtained from the condensation of pyridoxamine and 3--formyl-6-methylchromone; induces the formation of reactive oxygen species (ROS) and has an apoptotic and genotoxic potentiality. The compound thus exhibits anticancer activity (against ovary; cervix; brain and breast cancer); the mechanism of action possibly is via oxidative damage [40].

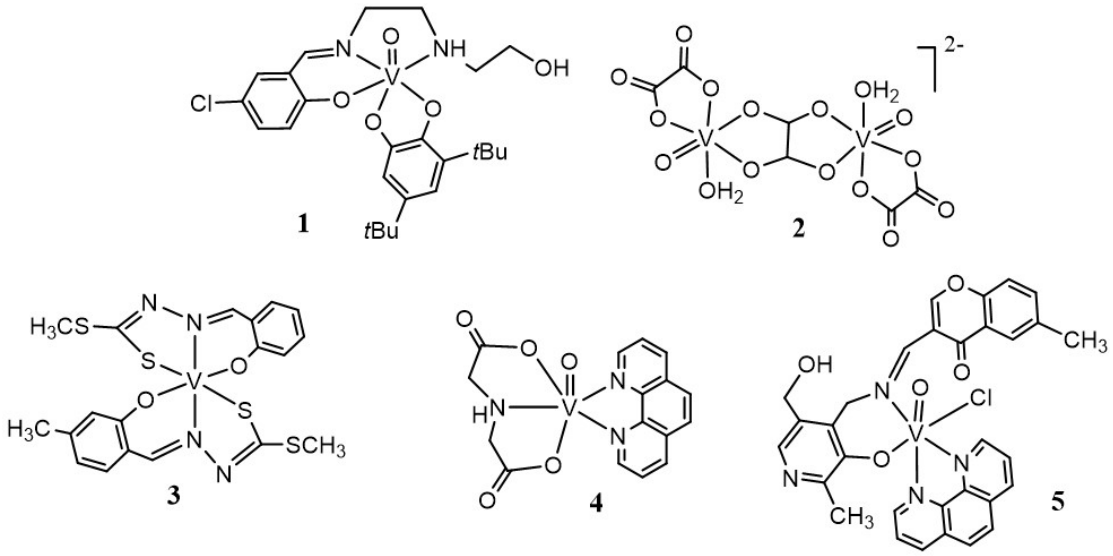


Figure 6: 1 [VO(dtb)(Hshed)] [the ligands are di(*tert*.-butyl)catecholate and N-(salicylideneaminato)-N′(2-hydroxyethyl)ethane-1;2-diamine] [36]. The water soluble complex 2 is cytotoxic [37]; 3 [38] has been assayed against colon cancer and cervical cancer (HeLa cells); 4 against hepatocellular carcinoma [39]; and 5 against ovary; cervix; brain and breast cancer [40].

Conclusion

An increased number of vanadium compounds has been investigated (essentially within the two bygone decades) with respect to their antibacterial effect and; in particular; related to their medicinal potentiality in the treatment of diabetes and various types of cancer; and also more recently; in view of their applicability in the medication of COVID-19. A plethora of these prospective medications is based on relatively complex (oxido)-V^{V} and -V^{IV} coordination compounds which – at physiological conditions; i.e. in contact with body fluids – undergo (partial) degradation to less complex species; including vanadate and; under reducing conditions; VO^{2+}·aq as the final metabolites. In contrast to other metal-ion based medications for the treatment of cancer (such as the well-established cisplatin); medicinal applications on the basis of vanadium drugs have so far not yet been officially admitted.

At least in part; vanadium coordination compounds present in the physiological broth; gradually decay to form VO^{2+}·aq and/or vanadate(V) as the final product – the latter being a phosphate analogue and consequently both a phosphate competitor/antagonist; *and* an intensifier of the action of phosphate – depending on the respective situation. The antagonism is due to vanadium's redox sensitivity and its ability to amplify its coordination sphere. Contrasting platinum; vanadium (in the form of vanadate and; under reducing conditions; oxidovanadium(IV)) is omnipresent – though at low (non-toxic) concentrations – in the body fluids and thus (at "normal" physiological concentrations) an "accepted life ingredient"; a fact which should further be considered in future applications of vanadium-based medicinal applications [40].

Data Availability Statement

All of the information and data included in this report have been taken from the publicly available original articles disclosed/cited in the present record.

References

1. (a) S Trevino, A Dias, E Sanchez-Lara, BL Sanchez-Gayta, JM Perez-Aguilar (2019) Biol0. Trace Elem. Res. 188: 68-98. (b) I Andersson, A Gorzsás, C Kerezsi, I Tóth, Dalton Trans (2005) 3658-66.

2. (a) KM Holtz, B Stec, ER Kantrovitz (1999) J Biol Chem, 274: 8351-4. – (b) I Persson, M Trublet; W Klysubun (2018) J Phys Chem A, 122: 7413-20. – (c) AS Samarin, IA Trussov, ZV Pchelkina, SS Fodotov, YA Ovchenkov (2023) Angew Chem, 63: e202316719.

3. (a) DR Davies,WGJ Hol, FEBS Lett, 577: 315-21. (b) KM Holtz, B Stec, ER Kantrowitz, J Biol. Chem; 274: 8351-4.

4. (a) CC McLauchlan, BJ Peters, GR Willsky, DC Crans, Coord (2021) Chem Rev, 163-99. – (b) SR Akabayov, B Akabayov (2021) Inorg Chim Acta, 420: 16-23.

5. AP Singh, S Roy, IC Maurya, Trans Met, Chem (2023) https://doi.org/10.1007/s11243-023-00565-4.

6. (a) MFA Santos; J Costa Pessoa (2023) molecules 28: 6535 – (b) DE Salazar Marcano; J-J Chen; MA Moussawi; G Kalandia; AV Anyushion; TN Parac-Vogt; J Inorg Biochem 260: 112687.

7. LMA Lima, H Murakami, DJ Gaebler, WE Silva, MF Belian et al. (2021) Inorganics, 9: 42.

8. (a) DC Barceloux, D Barceloux (1999) J Toxicol Clinic, 37: 265-78. (b) S Mahanty, D Raghav, K Rathinasamy (2021) J Biol Inorg Chem, 26: 511-31. (c) H Fan, K Dukenbayev, L Nurtay, F Nazir, N Daniyeva, TT Oham, E Benassi, J Inorg Biochem, 112619.

9. (a) A Gorzás, I Andersson, L Pettersson (2006) Eur J Inorg Chem, 3559-65. (b) B Mukherjee, B Patra, S Mahapatra, P Banerjee, A Tiwari, Toxicol Lett, 150: 135-43.

10. D Patra, A Pal, S Nath, MGB Drew, T Ghosh (2022) J Inorg Biochem, 234: 111900.

11. J Korbecki, I Baranowska-Bosiacka, I Gutawska, D Chlubek (2015) Int J Mol Sci, 16: 12648-168.

12. N McCann, M Imle, H Hasse (2015) Polyhedron, 95: 81-5.

13. J Costa Pessoa, MFA Santos, I Correiea, D Sanna, G Sciortino et al. (2021) Coord Chem Rev, 449: 214192.

14. A Scibior (2016) Chem Biol Interactions, 258: 214-33.

15. V Ugone, F Pisanu, E Garribba (2022) J Inorg Biochem, 234: 111876.

16. (a) S Das Baishnab, RN Dutta Purkayastha, W Maniukiewics, RM Comilla, A Frontera (2024) Inorg Cim Acta 559: 121770 (b) M Aureliano, NI Gumerova, G Sciortino, E Garribba, CC Mclauchlan, A Rompel (2022) Coord Chem Rev, 454: 214344.

17. (a) B Lyonnet, X Martz, E Martin (1899) La Press Medicale, 32: 191-2. (b) M Kumar, AM Singh, VK Singh, RK Yadav, AP Singh et al. (2024) Chem Rev, 505: 215663. (c) (d) H Huang, W Geng, X Wu, Y Zhang, L Xie et al. (2024) Angew Chem, 63: e202310811.

18. AL De Sousa-Coelho, G Fraqueza, M Aureliano (2024) Pharmaceuticals, 17: 12.

19. S Lim, JH Bae, HS Kwon, MA Nauk (2021) Nat Rev Endocrinol, 17: 11-30.

20. S Semiz (2022) J Trace Elem, Med Biol, 69: 126887.

21. D Favre, JF Harmon, A Zhang, MS Miller, IG Kaltashov (2022) J Inorg Biochem, 234: 111899.

22. JH McNeill, VG Yuen, S Dai, C Orvig et al. (1995) Mol Cell Biochem, 153: 175-80.

23. K Elvingson, AG Baró, L Pettersson (1996) Inorg Chem, 35: 3388-93.

24. Á Dörnyei, S Marcão, J Costa Pessoa, T Jakusch, T Kiss (2006) Eur J Inorg Chem, 2021: 3614-621.

25. (a) G Ferraro, M Paolillo, G Sciortino, E Garribba, A Merlino (2022) Inorg Chem, 16458-67. (b) K Küssner, V Ugone, D Sanna, M Cziferszky (2024) Inorg Chem, 63: 11785-7796. (c) D Sanna, M Serra, G Micera, E Garribba (2014) Inorg Chem, 53: 1449-64.

26. J Gätjens, B Meier, T Kiss, EM Nagy, P Buglyó et al. (2023) Chem Eur J, 9: 4924-35.

27. MR Maurya, M Nandi, PK Chaudhary, S Singh, F Avecilla et al. (2024) Inorg. Chem. 63 (2024) 714-729.

28. G Sahu, SA Patra, PD Pattanayak, W Kaminsky, R Dinda (2023) Inorg Chem, 62: 6722-39.

29. LMA: Lima, MF Belian, WE Silva, K Postal, K Kostenkova et al. (2021) J Inorg Biochem, 216: 111312.

30. A Jasińska, J Szklarzewicz, A Jurowska, M Hodorowicicz, G Kazek et al. (2022) 215 (2022) 115682.

31. G Ferraro, M Paolillo, G Sciortino, F Pisanu, E Garribba, A Merlino (2023) Inorg Chem, 62: 8407-17.

32. (a) AL De Sousa-Coelho, M Aureliano, G Fraqueza, G Serrão, J Gonçalves et al. (2022) 235: 111915. (b) T Aissa, D Aissaoui-Zid, W Moslah, O Khamessi, N Srairi-Abib et al. (2024) J Inorg Biochem, 260: 112672.

33. E Kioseoglou, S Petanidis, C Gabriel, A Salifoglou (2015) Coord Chem. Rev, 87-105.

34. Z Arhouma, HA Murakami, JT Koehn, X Li, DA Roess et al. (2022) Inorganics, 10: 50.

35. HA Murakami, C Uslan, AA Haase, JT Koehn, AP Viera et al. (2023) Inorg Chem, 61: 20757-73.

36. GB Baptisella, GCM Manica, SW de Souza, FS Santana, LC Fachini et al. (2023) Polyhedron, 198: 115071.

37. A Banerjee, SA Patra, G Sahu, G Sciortino, F Pisanu et al. (2023), Inorg Chem 62: 7932-53.

38. L Ni, W Chang,S Zhu, Y Zhang, P Chen et al. (2021) ACS Appl Bio Mater, 4: 8571-83.

39. P Nunes,Y Yildizhan, Z Adiguzel, F Marques (2022) J. Costa Pessoa; C. Acilan; I. Correia; J. Biol. Inorg. Chem 27 (2022) 89-109.

40. N Ribeiro, I Bulut, V Pósa, B Sergi (2022) J Inorg Biochem, 235: 111932.