

# Chapter 18

## Vanadium-Based Transformations Effected by Algae and Microbes



Dieter Rehder

**Abstract** Many algae and bacteria living in either aquatic or terrestrial environments are capable of transforming and in many ways utilizing inorganic vanadium—essentially vanadate(V) and oxidovanadium(IV)—in bio-transformations. These metabolic activities often are based on redox interactions between  $V^V$  and  $V^{IV}$  (and sometimes  $V^{III}$ ). Examples are (1) the oxidation of halides and pseudohalides by marine phytoplankton such as macroalgae (seaweeds), (2) the fixation of nitrogen (conversion of  $N_2$  to  $NH_4^+$ ) and the hydrogenation of alkynes by bacteria belonging to the genus *Azotobacter* and by cyanobacteria associated with bryophytes, and (3) the respiratory and dissimilatory reduction of  $H_2VO_4^-$  to  $V^{IV}$  (commonly insoluble  $VO(OH)_2$ ). Vanadate reduction can further be coupled with the nitrate to nitrite reduction process by *Thioalkalivibrio nitratireducens*, and to the oxidation of methane. Vanadate-reducing bacteria are of particular ecological interest for industrial areas where vanadium ores are processed with the release of (toxic) vanadate: Bacterially induced reduction of vanadate to insoluble  $VO(OH)_2$  is an increasingly probed object of research. In addition, bacterial reduction of vanadate does have implications in microbial fuel cells. Along with  $H_2VO_4^-/VO^{2+}$ , vanadium coordination compounds can exhibit antimicrobial activities related to health issues such as bacterial pneumonia. Decavanadate notably exerts growth inhibition against *Escherichia coli*.

### 18.1 General Role of Vanadium: Occurrence, Toxic and Beneficial Effects

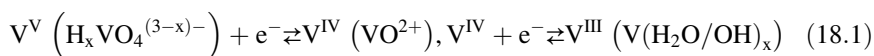
Vanadium, the 20th most abundant element on Earth, occurs in about 70 variants of minerals, in the form of oxidovanadium(IV) ( $VO^{2+}$ , “vanadyl”) in the porphyrins in crude oil and shales, and as hydrogenvanadate ( $H_2VO_4^-$ ) in water reservoirs. The concentration of vanadate in seawater (where vanadate is an essential source for

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macro-algae and several sea organisms, tunicates and fan worms in particular) amounts to an average of ca. 35 nM. Vanadate ( $\text{H}_x\text{VO}_4^{(3-x)-}$ ,  $x = 1$  or 2, depending on the pH at about physiological conditions) is omnipresent in groundwater. Reductive processes can convert—and thus detoxify—vanadate into insoluble  $\text{VO}(\text{OH})_2$ .

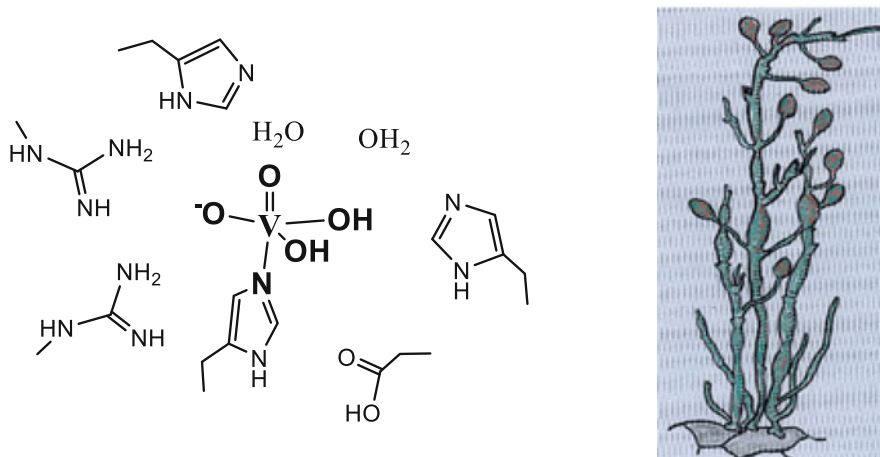
In either oxidation state,  $\text{V}^{\text{V}}$  and  $\text{V}^{\text{IV}}$  (and  $\text{V}^{\text{III}}$ ), vanadium can enter cellular compartments: in the form of vanadate via phosphate channels, and in the form of  $\text{VO}^{2+}$  via transport by transferrin. Supposedly, hydrogenvanadate—in trace amounts—is an essential element for the majority of living organisms. In part, this is due to its structural (and, to some extent, its chemical) similarity to hydrogen phosphate, a resemblance that induces—via its interference with physiologically relevant components—competitive behaviour in metabolic processes that are commonly governed by phosphatases and kinases. However, contrasting phosphate, vanadate(V) is labile with respect to reduction to  $\text{V}^{\text{IV}}$  ( $\text{VO}^{2+}$ , commonly in the form of VOL, where L is a biogenic ligand) and further to  $\text{V}^{\text{III}}$ , Eq. (18.1).



This redox lability makes vanadate more versatile than phosphate—but to some extent also potentially hazardous with respect to its functions in life: Vanadate is a competitor of phosphate, and vanadyl is a competitor of biologically relevant transition metal(2+) ions, which means that these vanadium ions can cause objectionable physiological side effects, and those effects potentially are ecotoxic. Another striking difference between vanadate and phosphate is the ability of vanadium (in all of its oxidation states) to attain the coordination numbers five, six (and even seven, in the vanabins of *Amanita* mushrooms), while phosphorous in phosphate at best undergoes intermediate and weak interactions with a fifth electron donor.

## 18.2 Oxidative Transformation of Halides and Pseudohalides by Vanadate-Dependent Haloperoxidases

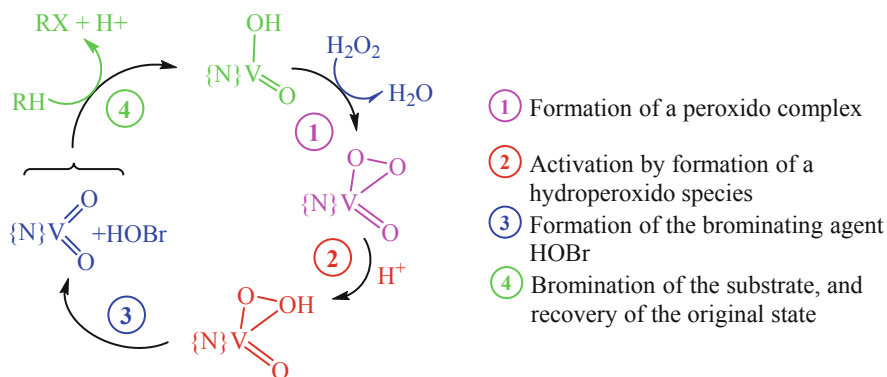
Haloperoxidases catalyze the oxidative (normally by peroxide) transformation of halides, and usually pseudohalides as well, to hypohalous acid (hypohalite) that further are involved in the halogenation of organic substrates; Eq. (18.2a and 18.2b). Vanadate-dependent haloperoxidases (VHPOs) rely on hydrogenvanadate  $\text{H}_2\text{VO}_4^-$  bound into the catalytically active centre of the enzyme via a histidine- $\text{N}^{\text{e}}$ , plus hydrogen bonding interaction with additional N- and O-functional amino acid residues (Fig. 18.1). These peroxidases have been isolated from marine macroalgae (brown algae in particular, e.g. *Ascophyllum nodosum*; Fig. 18.1) (Vilter 1983, 1984; Wever et al. 2018), saprobes (such as the fungus *Curvularia inaequalis*) (Messerschmidt and Wever 1996), and from the terrestrial lichen *Xanthoria*



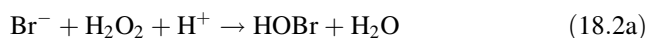
**Fig. 18.1** The active centre  $\text{H}_2\text{VO}_4(\text{His})^-$  (in bold) of the vanadate-dependent haloperoxidase of *Ascophyllum nodosum* (shown on the right), including a selection of nearby amino acid residues. In its inactive state, vanadium is in a distorted square pyramidal environment (McLauchlan et al. 2018). The central part (in bold) is conserved in all VHPOs; the second sphere (in hydrogen-bonding contact with the inner sphere) is subject to variations and responsible for the substrate specificity ( $\text{I}^-$ ,  $\text{Br}^-$ ,  $\text{Cl}^-$ , pseudohalides)

*parietina* (Plat et al. 1987). Vanadate-dependent iodoperoxidases are also present in some species of cyanobacteria (Bernroither et al. 2009); see also further down. Haloperoxidases “oxidatively” protect the algae against *parasitic* bacteria. More generally, many bacterial strains are sensitive to oxidative annihilation by hypohalite generated vanadium chloroperoxidase. An example is an antimicrobial effect against *Enterococcus faecalis* biofilms (Persoon et al. 2011). However, vanadate-dependent peroxidases can also be present in specific bacteria. Examples thereof include a chloroperoxidase detected in marine *Streptomyces* bacteria (Bernhardt et al. 2011; McKinnie et al. 2018), in cyanobacterial blooms responsible for the formation of halogenated methane derivatives (Johnson et al. 2015), and in flavobacteria associated with marine macroalgae (Fournier et al. 2014). The flavobacterium *Zobiella galactanivorans* (a marine bacterium associated with macroalgae) contains monomeric iodoperoxidases; more generally, the monomeric type of VHPOs is overrepresented in bacterial lineages. VHPOs likely derive from a marine bacterial ancestor; they are closely related to bacterial acid phosphatase (Fournier et al. 2014).

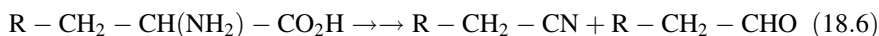
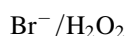
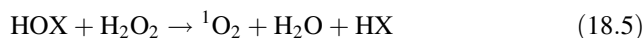
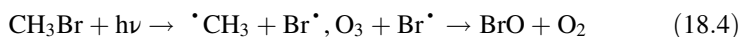
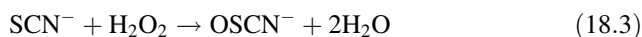
The active centre of these haloperoxidases is illustrated in a generalized form in Fig. 18.1. Figure 18.1 also pictures the brown alga *Ascophyllum nodosum*, where the enzyme has originally been detected and characterized (Vilter 1983, 1984). The active centre of the peroxidase in Eq. (18.1a) is symbolized by  $\{\text{H}_2\text{VO}_4^-\}$ . The mechanism of the halide peroxidation catalyzed by VHPOs is emblemized in Fig. 18.2.



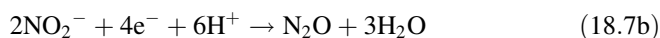
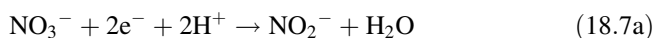
**Fig. 18.2** Mechanistic aspects of the bromination of an organic substrate (RH) by vanadium-based bromoperoxidase. The active centre is symbolized here by “ $\{N\}VO(OH)$ ” (top), where  $\{N\}$  stands for the directly ligated histidine (see Fig. 18.1) from the protein matrix



Along with halides, pseudohalides can also be subject to oxidative transformation by the haloperoxidases of marine phytoplankton. An example is the oxidation of thiocyanate to hypothiocyanite, Eq. (18.3). The formation of hypohalous acid in a marine environment does also have an impact on atmospheric chemistry: bromomethane, e.g., when released into the atmosphere, undergoes photolytic degradation to form bromine radicals, which can react with ozone and thus attribute to the atmospheric depletion of the ozone layer, Eq. (18.4) (Wever et al. 2018). Similarly, chloroform  $CHCl_3$  generated from organics by the enzymatically steered generation of  $HClO$  is split photolytically to form chlorine radicals. Additionally, initiated by the reaction of hypohalous acid and hydrogen peroxide, highly reactive singlet oxygen can be formed at higher pH, Eq. (18.5). The latter is likely the responsible oxidant in the peroxidase-catalyzed oxidative (by  $H_2O_2$ ) decarboxylation of amino acids such as phenylalanine, Eq. (18.6) (But et al. 2012).

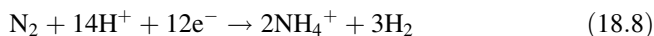


Haloperoxidase activity has also been detected for the (halo)alkaliphilic sulphur bacterium *Thioalkalivibrio nitratireducens*—living at extremely high pH and salinity (soda lakes). The main substrate for this chemolithoautotrophic bacterium, containing vanadium rather than molybdenum in its active centre, is the reduction of nitrate to nitrite (which can further be reduced to  $\text{N}_2\text{O}$ ), Eqs. (18.7a and 18.7b) (Antipov et al. 2003); electron donor is thiosulfate. Other substrates for the enzyme include chlorate, bromate, selenite and sulphite. The active centre of this periplasmic enzyme—a homotetramer of molecular mass 220 kDa—presumably contains three haeme-c groups and one vanadium. Other vanadate-reducing denitrifiers include *Pseudomonas isachenkovii* (Antipov et al. 1998). Additional substrates are, inter alia,  $\text{ClO}_3^-$ ,  $\text{BrO}_3^-$ ,  $\text{SeO}_4^{2-}$  and  $\text{SO}_3^{2-}$ .

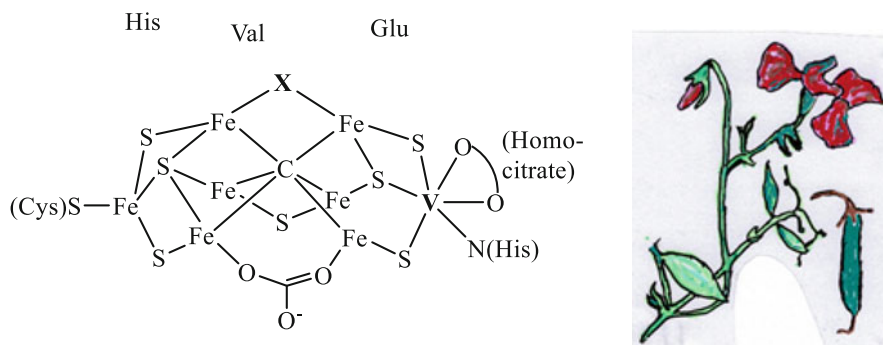


### 18.3 Hydrogenation of Unsaturated Substrates by Vanadium-Dependent Nitrogenase

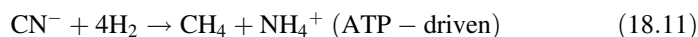
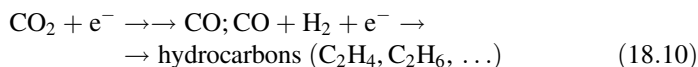
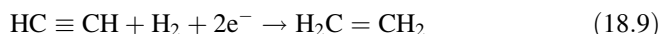
The nitrogen-fixing rhizobium bacterium *Azotobacter vinelandii* is responsible for the (proton- and ATP-supported) conversion of the comparably inactive (aerial) dinitrogen  $\text{N}_2$  to ammonium ions  $\text{NH}_4^+$ , and hence into a nitrogen source indispensable for a plethora of organisms for the synthesis of organic nitrogen compounds serving as building blocks for, e.g., amino acids and hence proteins. *A. vinelandii* is a soil bacterium, living symbiotically in the root nodules of members of the legume family (*Fabaceae*) such as clover, beans and sweet peas (e.g. *Lathyrus*, Fig. 18.3, right). The enzymes responsible for this ATP-driven conversion of  $\text{N}_2$  to  $\text{NH}_4^+$ , the nitrogenases, are comparatively complex iron-vanadium (or iron-molybdenum, or iron-only) proteins (Fig. 18.3, left); for the overall reaction see Eq. (18.8). The uptake of vanadate (and/or molybdate) is initiated by the siderophore azotobactin (Wichard et al. 2009).



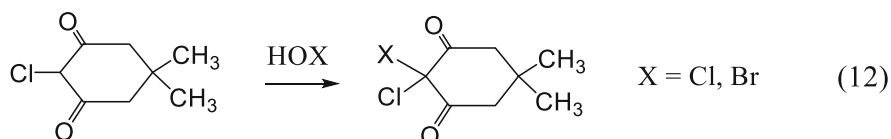
Other unsaturated basic molecules, such as acetylene (Eq. 18.9),  $\text{CO}_2/\text{CO}$  (Eq. 18.10), and cyanide (Eq. 18.11) (Sippel and Einsle 2017; Sickerman et al. 2017) may equally be substrate for a reductive conversion based on vanadium-dependent nitrogenase. The reduction of  $\text{CO}$  by nitrogenases (Lee et al. 2018) is of particular interest in as far as  $\text{CO}$  and  $\text{N}_2$  are isoelectronic.



**Fig. 18.3** The iron-vanadium cofactor (M-cluster) of the vanadium nitrogenase from *A. vinelandii* (adapted from Benediktsson et al. 2018, modified). The bridging X can represent particularly labile  $S^{2-}$ , or OH, NH (Sippel et al. 2018), HCN,  $CN^-$ ,  $N_3^-$ , and CO (Eq. 18.10) (Rohde et al. 2020), and  $HC \equiv CH$  (Eq. 18.9), depending on the state of activation and on the substrate. The six irons surrounding the central carbon are arranged as a trigonal prism. The picture on the right represents the flour and fruit of *Lathyrus* (sweet pea), a member of the legume family



Along with *A. vinelandii*, associated with the legume family, the lichen-symbiotic cyanobacteria from the genus *Nostoc*, associated with lichen-forming fungal species of the genus *Peltigera*, contain (commonly along with a molybdenum and iron-only nitrogenase) a vanadate-dependent nitrogen fixing system that also catalyzes acetylene reduction (Hodkinson et al. 2014). Further, cyanobacteria (such as *Nostoc sp.*) associated with bryophytes (liverworts and hornworts) have been shown to employ—in addition to molybdenum nitrogenase—vanadium-nitrogenase (Nelson et al. 2019). As mentioned above, *Streptomyces* bacteria can also be involved—resorting to vanadate-dependent chloroperoxidase—in the biosynthesis of halogenated meroterpenoid products (McKinnie et al. 2018). An example is the chlorination/bromination of monochlorodimedone; Eq. (18.12).

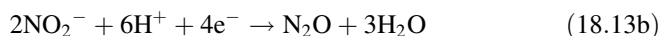
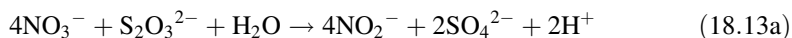


## 18.4 Accumulation and Redox Transformation of Vanadate(V) and Oxidovanadium(IV) by Bacteria and Protozoa

Several bacteria, archaea and fungi are able to reduce soluble vanadium (V) (hydrogenvanadate) to insoluble vanadium(IV) (commonly oxidovanadium hydroxide), eventually followed by geogenic conversion, i.e. formation of vanadium minerals. The reduction can be respiratory (the electron flow is coupled to the translocation of protons) or dissimilatory (anaerobic respiration; a proton-motive force is not involved). In tunicates, the reduction of vanadate is coupled to a symbiotic bacterium which previously was assigned the temporary name of *Pseudomonas isachenkovii* (Lyalkova and Yukova 1990; Lyalikova and Yukova 1992).

Intracellular and cell surface bioaccumulation of vanadium(V) and -(IV) (in concentrations up to 0.67 mM) by vanadium-resistant bacterial strains have been noted for the intestines of *Ascidia sydneiensis samea* (Romaidi 2016). The bacteria belong to the genera *Vibrio* and *Shewanella*. The maximum absorption (at pH 3) corresponds to an enrichment of twenty thousand times that of vanadate in seawater. A more recent study by Ueki et al. (2019) examined and compared the symbiotic bacteria (such as *Pseudomonas* and *Ralstonia*) associated with vanadium-rich ascidians (*Ascidia ahodori* and *A. sydneiensis samea*, with vanadium particularly accumulated in the branchial sacs) versus vanadium-poor ascidians (*Styela plicata*).

The chemolithoautotrophic bacterium *Thioalkalivibrio nitratireducens* has available a nitrate/nitrite reductase containing vanadium and haeme-c as cofactors (a homotetramer of the molecular mass 195 kDa; four identical subunits) (Antipov et al. 2003; Antipov 2013). Nitrate is reduced to nitrite and further to N<sub>2</sub>O (Eqs. 18.13a and 18.13b); electron donor is thiosulfate. *T. nitratireducens* is alkaliphilic and moderately halophilic, i.e. it exists at high pH and salinity (high soda levels). Substrates other than NO<sub>3</sub><sup>-</sup> include ClO<sub>3</sub><sup>-</sup>, BrO<sub>3</sub><sup>-</sup>, SeO<sub>4</sub><sup>2-</sup>, and SO<sub>3</sub><sup>2-</sup>. Interestingly, this enzyme does also have haloperoxidase activity (see above).

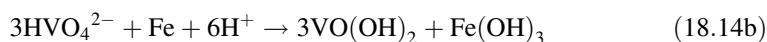


Microbial vanadate reduction (by *Methylomonas*) in particular in groundwater can also be coupled with anaerobic methane oxidation. The oxidation products are CO<sub>2</sub> along with fatty acids (Zhang et al. 2020); for a net reaction leading to fatty acids see Eq. (18.14a). Further reduction can result in the generation of methane. Nitrate essentially inhibits vanadate reduction, likely because (less toxic) nitrate is preferentially employed by the bacteria. Electron transfer to vanadate may occur directly, or via binding of vanadate to reductases of other electron acceptors, such as

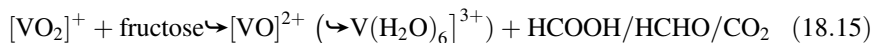
NADPH-dependent reductase. A similar situation applies to the competitive—vanadate vs. nitrate—behaviour in the bio-reduction of hydrogen (Jiang et al. 2018).



Vanadate(V)-reducing bacteria include the genera *Bacillus*, *Geobacter*, *Clostridium*, *Pseudomonas*, and the *Comamonadaceae* (a Gram-negative bacterial family commonly equipped with a flagella). Vanadate, at moderate to low concentrations, can effectively promote the growth of these bacteria (Wang et al. 2020). These bacterial strains dispose of a comparatively high vanadium resistance. An example is *Bacillus megaterium* (Rivas-Castillo et al. 2017). Since high concentrations of vanadate in the surface soil mainly of industrial areas are considered to exert ecological risks and, where appropriate, toxic effects [as noted previously, vanadate is an antagonist of phosphate], bacterial detoxification by reduction of  $\text{H}_2\text{VO}_4^-$  to  $\text{VO}^{2+}$ , and precipitation of the latter in the form of  $\text{VO}(\text{OH})_2$ , is ecologically (and consequently economically as well) important. Interestingly, elemental iron and sulphur can also reduce vanadate(V), in the presence of hydrogen carbonate and ammonium ions, to form insoluble vanadium(IV) hydroxide; see Eq. (18.14b) for the reduction by iron (Zhang et al. 2018). Bacteria responsible for these reductions belong to the strains *Geobacter* (for the reduction by iron) and *Spirochaeta* (for the reduction of sulphur).

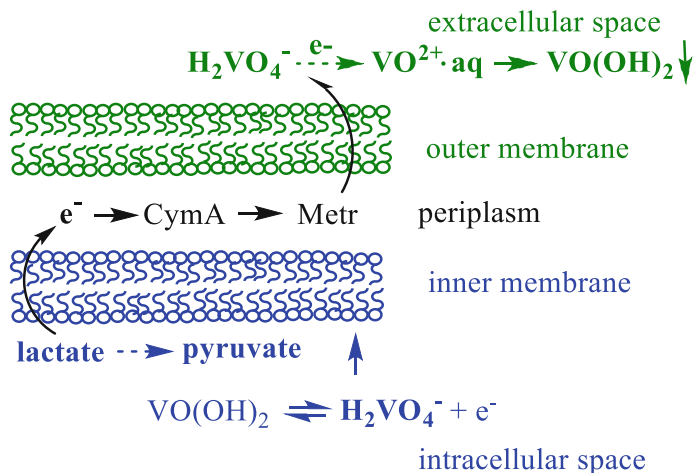


The acidophilic obligatory heterotrophic bacterium *Acidocella aromatica* reduces vanadium(V) ( $\text{H}_2\text{VO}_4^-$ ), using fructose. Reduction takes place under microaerobic as well as anaerobic conditions, at vanadate concentrations up to 2 mM. Reduction is effective even under highly acidic (pH 2) conditions (Okibe et al. 2016) (where vanadium is present in the form of  $[\text{V}^{\text{V}}\text{O}_2(\text{H}_2\text{O})_4]^+$ ), and the potential oxidation products are formic acid, formaldehyde and  $\text{CO}_2$ , Eq. (18.15). The final (subtoxic) vanadium concentration is  $\sim 10 \mu\text{M}$ , hence a decrease of  $c(\text{V})$  by two orders of magnitude. The reduction product is blue  $\text{V}^{\text{IV}}\text{O}^{2+}\cdot\text{aq}$  (which, in part, can be further reduced to V(III)). With increasing pH, oxidovanadium hydroxide  $\text{VO}(\text{OH})_2$  precipitates, and temporarily becomes absorbed to the bacterial surface.

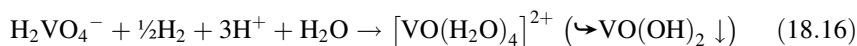


Bioreduction of vanadate(V) present in ground water, at about neutral pH and temperatures in the range between 15 and 40 °C, is also achieved by autohydrogenotrophic bacteria belonging to the  $\beta$ -proteobacteria such as *Rhodocyclus* (a denitrifying bacterium) and *Clostridium* (a fermenter); hydrogen gas  $\text{H}_2$  is used as the electron donor (Xu et al. 2015), Eq. (18.16).



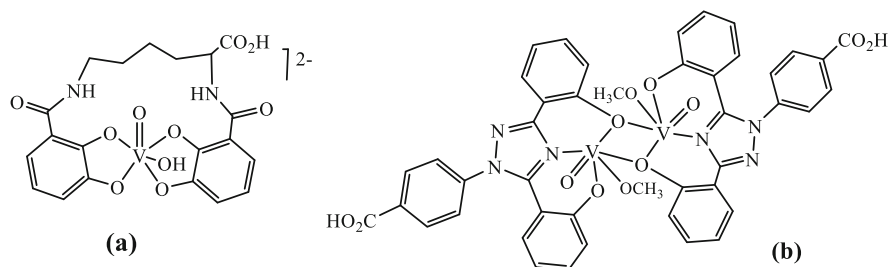


**Fig. 18.4** Electron transport from the intra-cellular to the extra-cellular space, exemplified for lactate as electron donor. CymA and Metr are heme-type iron proteins associated with the inner (CymA) and the outer (Metr) membrane. The main amount of vanadate is refined to the *extracellular* space

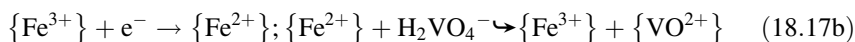
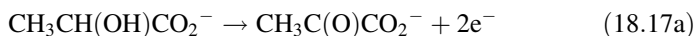


The potentiality of metal ion reduction (and vanadate in particular) by microbes such as *Geobacter metallireducens*, *Shewanella oneidensis*, *Pseudomonas*, *Lactococcus* and *Enterobacter* in (ground) water reservoirs (Ortiz-Bernard et al. 2004; Carpentier et al. 2005) has also been applied in microbial fuel cells to generate “bio-electricity”, and concomitantly detoxify groundwater (Hao et al. 2015). Organic substrates such as glucose and acetate effectively enhance microbial growth, *Lactococcus* (a lactic acid bacterium) being particularly effective in vanadate reduction.

The vanadium(V) reductase activity of bacteria takes place in the bacterial membrane, and is indirectly coupled to the oxidation of  $\text{H}_2$  or organics such as sugars and organic acids (e.g. lactate; Eq. 18.17a), and thus links carbon metabolism to the reduction of vanadate (and commonly other inorganics such as  $\text{Fe}^{3+}$  and  $\text{Mn}^{4+}$  as well) (Dundas et al. 2018, 2020). The  $\text{Fe}^{3+}/\text{Fe}^{2+}$  centres in the cytochrome-c type proteins CymA and MetrABC are involved in the transmembrane electron pathway, Eq. (18.17b): As illustrated in Fig. 18.4, electrons are delivered via the inner membrane by, e.g., lactate, to CymA( $\text{Fe}^{3+}$ ) to form CymA( $\text{Fe}^{2+}$ ). Further electron transport across the periplasm and the outer membrane involves MetrABC( $\text{Fe}^{3+}/\text{Fe}^{2+}$ ). The cytochromes have been symbolized, in Eq. (18.17b), by  $\{\text{Fe}^{3+}\}$  and  $\{\text{Fe}^{2+}\}$ . The reduction equivalents are finally taken up by extracellular hydrogenvanadate. Figure 18.4 provides an overview for this electron transfer pathway.



**Fig. 18.5** (a) Probable structure of the complex formed between oxidovanadium(V) and azotocheline. (b) A dinuclear antiamoebic vanadium complex with the ligand deferasirox (a medication commonly used to counteract iron overload in the blood)



Relating to vanadium-dependent nitrogenase (vide supra), the biosynthesis of the bis(catecholate) azotocheline by the soil bacterium *Azotobacter vinelandii* is of interest: azotocheline forms a strong coordination compound with  $\text{VO}^{3+}$  (Fig. 18.5a), a complex which supposedly acts as a vanadophore in supplying *A. vinelandii* with vanadium (Bellenger et al. 2007). Along with the bacterial reduction of vanadate(V) to oxidovanadium(IV) and thus insoluble  $\text{VO}(\text{OH})_2$ , further reduction of  $\text{VO}(\text{OH})_2$  to soluble  $[\text{V}^{\text{III}}(\text{OH})_{2/1}(\text{H}_2\text{O})_{4/5}]^{3+}$  has been noted to be performed, in hydrothermal environments, by several bacterial strains, such as *Pseudomonas aeruginosa* (Baysse et al. 2000).

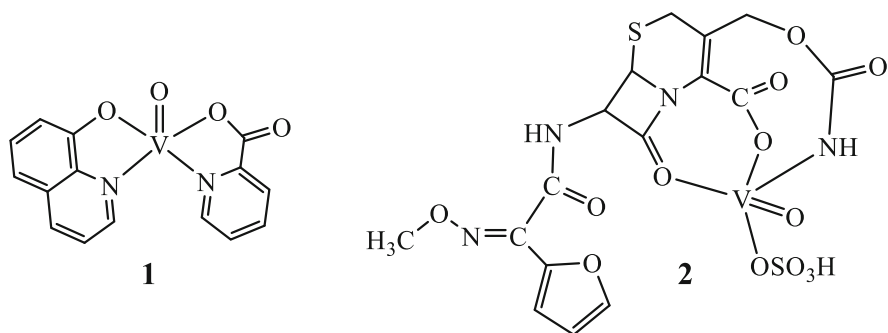
Not surprisingly, bacteria can also be involved in the transformation of inorganic vanadium compounds. An example is the reductive conversion (and thus “detoxification”), by *Geobacter sulfurreducens*, of  $\text{V}^{\text{V}}$ -bearing ferrihydrites/magnetites. In this reaction, nano-particulate vanadium ferrite spinel  $(\text{Fe}, \text{V})_3\text{O}_4$  is produced (Coker et al. 2020; Liang et al. 2010), with a  $\text{V}^{\text{IV}}/\text{V}^{\text{III}}$  ratio around 0.3, and the iron (partially) reduced to  $\text{Fe}^{\text{II}}$ . These vanadium-substituted magnetites, with V predominantly at  $\text{Fe}^{\text{III}} \text{O}_h$  sites, are likely to have a potential as catalysts in electron transfer processes, e.g. in organic reactions. More generally, bacterial reduction of vanadium (V) to vanadium (IV) is an important issue as a response to vanadium pollution in the wake of mining and processing vanadium ores such as navajoite  $\text{Fe}^{\text{III}}\text{V}^{\text{V}}_9\text{O}_{24} \cdot 12\text{H}_2\text{O}$  (Wang et al. 2020).

## 18.5 Antimicrobial Effects of Vanadium Coordination Compounds

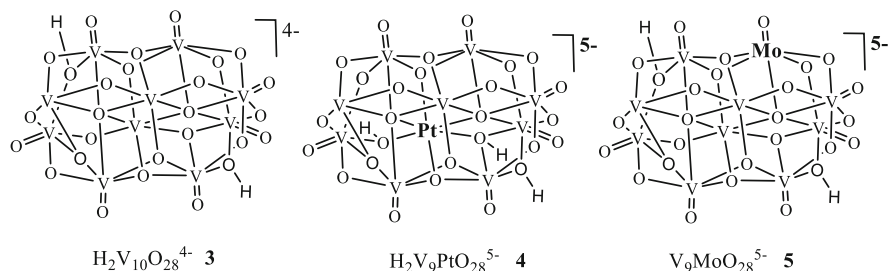
In conjunction with the bacterial *use* of vanadium (commonly, as noted above, in the form of vanadate(V) or oxidovanadium(IV)), *antibacterial* activity and interaction with unicellular organisms (protozoans) such as amoebae is of interest. A well-studied example is the antiamoebic activity (against *Entamoeba histolytica*) of specific vanadium coordination compounds such as the bis(oxidovanadium(V)) complex formed with deferasirox (4-[3,5-bis(2-hydroxyphenyl)-1,2,4-triazol-1-yl] benzoic acid; Fig. 18.6) (Maurya et al. 2016). That compound is more potent than the amoebicidal standard drug metronidazole.

Selected examples of vanadium coordination compounds that have turned out to be auspicious in antimicrobial (and antiviral) applications are depicted in Fig. 18.6.  $V^{IV}O(pic)(8HQ)$  (pic = picolinate, 8HQ = 8-hydroxyquinoline; **1** in Fig. 18.6) has been shown to counteract *Mycobacterium tuberculosis* (Correia et al. 2014), while the oxidovanadium(IV) complex VO(cefuroxime) (**2** in Fig. 18.6) exhibits antimicrobial activity against, e.g., pneumonia of bacterial origin, such as caused by *Klebsiella pneumoniae* (Datta et al. 2015). A likely mechanism of action of compound **1** is a release of the ligand at physiological conditions, causing binding (and thus depletion) of intracellular iron. The mechanism of action of compound **2** possibly roots in the hydrophobic interaction (docking through hydrophobic forces) between the vanadium complex and the protein receptor clathrin.

Along with mononuclear vanadium complexes, decavanadates such as depicted in Fig. 18.7, can have antimicrobial activity. The decavanadate **3** (with nicotinamide as the counter-ion) exerts growth inhibitory activity against *Escherichia coli* (Missina et al. 2018), the platinum and molybdenum substituted decavanadates **4** and **5** inhibit the growth of *Mycobacterium smegmatis* (Kostenkova et al. 2021) a generally non-pathogenic bacterium located in the genital areas.



**Fig. 18.6** Examples of antimicrobial vanadium complexes: Compound **1** is effective against tuberculosis, compound **2** against bacterial pneumonia



**Fig. 18.7** Decavanadate (left) (Missina et al. 2018) and substituted decavanadates (centre and right) (Kostenkova et al. 2021) that have been shown to exert antimicrobial activity. The counterions of compound **3** are nicotinamide and isonicotinamide

Similarly, octadecavanadates (IV/V) of composition such as  $[\text{V}^{\text{IV}}_{12}\text{V}^{\text{V}}_5\text{O}_{42}]^{7-}$  have been shown to exert chemo-protective activity, in *E. coli* cultures, towards alkylation by diethyl sulfate (Postal et al. 2021).

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