Integrated Risk Information System (IRIS) Program Public Science MeetingTopic #2: Consideration of vanadium speciation.

By Debbie C. Crans; Colorado State University

For developing *the* ***Populations, Exposures, Comparators and Outcomes (PECO) criteria for Vanadium*** with the ultimate goal of ***setting guidelines for safe limits in drinking water***

Disclaimer

- I do not have any financial relationships with persons or organizations having an interest in a toxicological review of vanadium compounds.
- No interested party had reviewed the input I am providing at the meeting today.

Topic: Consideration of vanadium speciation.

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For developing *the Populations, Exposures, Comparators and Outcomes (PECO) criteria for Vanadium* with the ultimate goal of *setting guidelines for safe limits in drinking water*

Chemical Speciation (slides 1-15)

- **Illustrate and define speciation**
- **Fundamental chemical and physical properties**
- **Speciation profile and Pourbaux diagrams**

Biological effects of speciation (slides 16-19)

- **Speciation cause different biological effects**

[a] **Differences in uptake by vanadium(V) and vanadium(IV)**

Future and recommendations with measurements (slides 20-21)

- **Methods to measure V-content and speciation**

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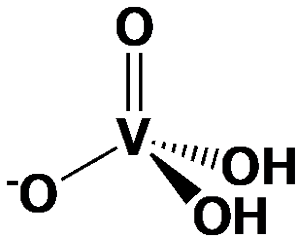
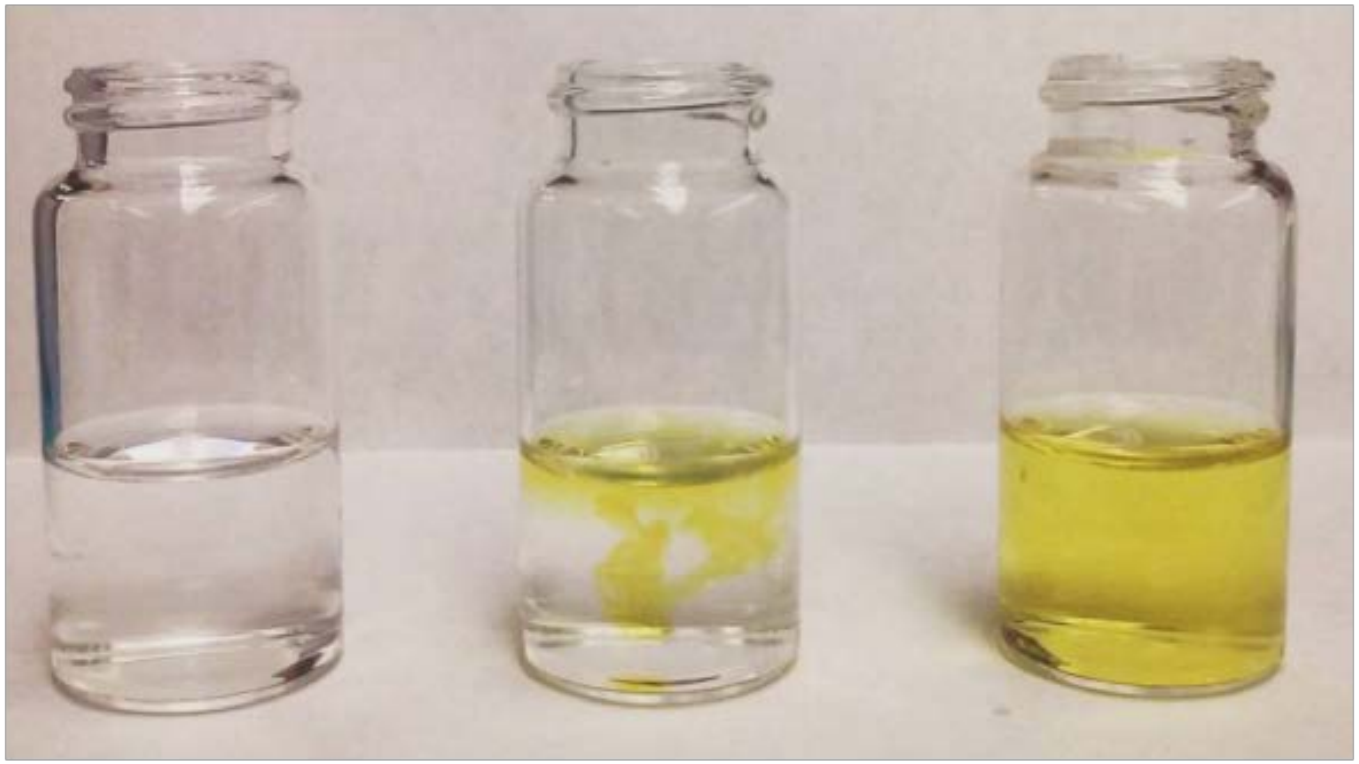
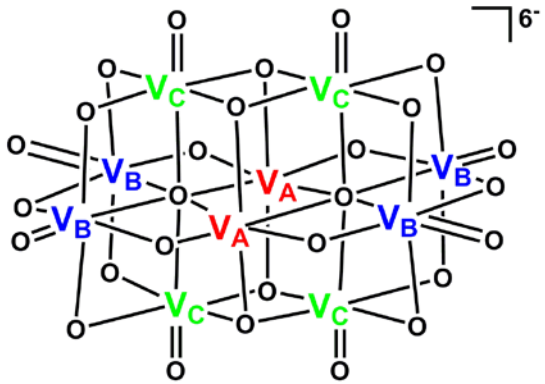
Illustration of speciation.

Vanadate and decavanadate - composition the same – pH different







Vanadate (pH 7) **Decavanadate (pH 3)**

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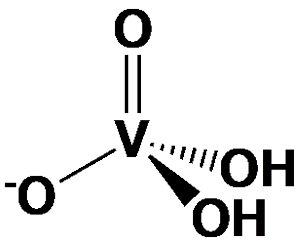
Definition and illustration of speciation.

Definition of speciation (in chemistry)

Table 1. Recommended IUPAC Speciation Definitions[9]

term	IUPAC definition
chemical species	chemical elements: specific form or an element defined as to isotopic composition, electronic or oxidation state, and/or complex or molecular structure
speciation analysis	analytical chemistry: analytical activities of identifying and/or measuring the quantities of one or more individual chemical species in a sample
speciation of an element (speciation)	distribution of a component among defined chemical species in a system

Crans, *Inorg. Chem.*, **2013**, *52*, 12264-12275



Vanadate and decavanadate - composition the same – pH different

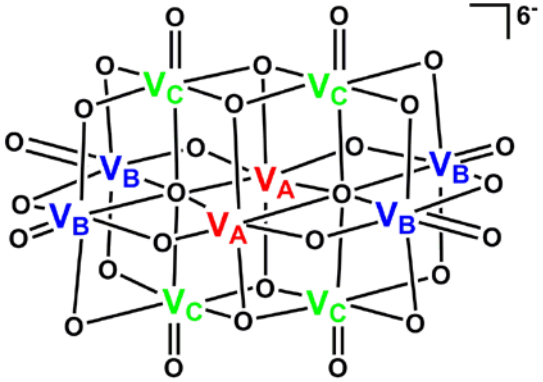
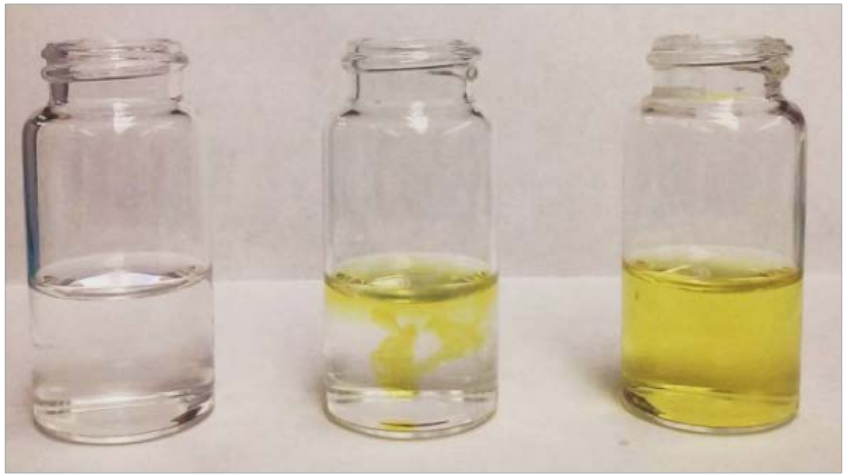


Illustration of speciation

Crans et al. *Chem. Rev.* 2004, 104, 849-902

Aureliano & Crans, *J. Inorg. Biochem.*, **2009**, *103*, 536-546



Vanadate (pH 7) **Decavanadate (pH 3)**

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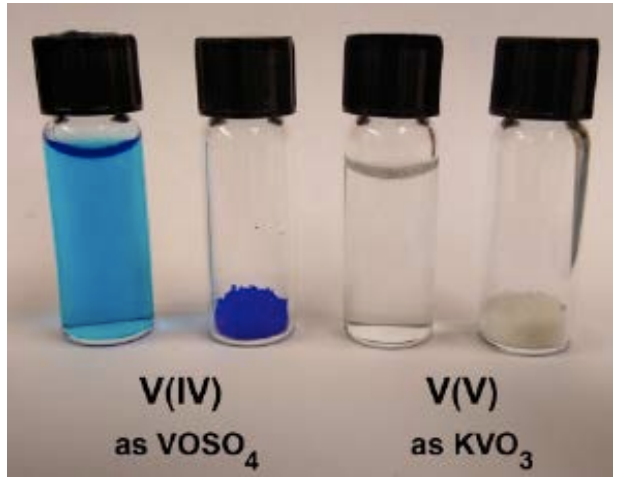
Topic: Consideration of vanadium speciation.

Vanadium Compounds:

Vanadium metal
Vanadium salt (Inorganic salts) - focus of todays work
Vanadium coordination complexes



Four classes of reactions result in diversity of compounds:

- Hydrolysis (reaction of solid with water)
- Acid – Base – protonation – deprotonation reactions
- Condensation - oligomerization reactions
- Redox reactions

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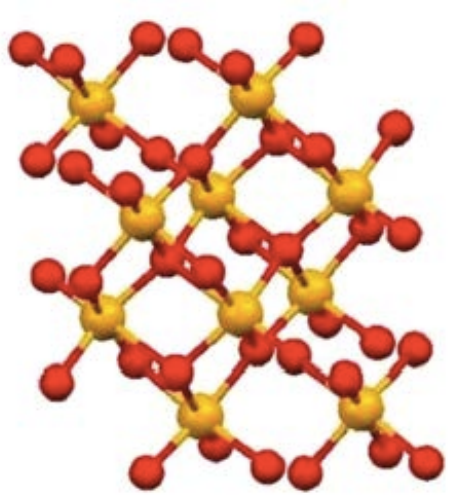
Materials Presented in draft report

Structures are shown with regard to what is reported in the **solid state**

V_2O_5 is a polymeric sheet that falls apart upon dissolution



Filonenko et al. Acta Crystallogr., Sect. B: Struct. Sci., 2004, 60, 375–381.
Haber et al. App. Cat. A: General, 1997, 157, 3-22

Table 1. Chemical identity and physiochemical properties of selected vanadium compounds as curated by EPA's CompTox Chemicals Dashboard

Name	Elemental vanadium	Vanadyl sulfate	Sodium metavanadate	Ammonium metavanadate	Sodium orthovanadate	Vanadium pentoxide
CASRN	7440-62-2	27774-13-6	13718-26-8	7803-55-6	13721-39-6	1314-62-1
DTXSID[a]	2040282	4021428	3044336	1052533	2037269	2023806
Structure						
Molecular weight (g/mol)	50.942	163	121.928	116.978	183.907	181.878
Molecular formula	V	$VOSO_4$	$NaVO_3$	NH_4VO_3	Na_3VO_4	V_2O_5
Selected Synonym(s)	Vanadium	(Oxido)vanadium(2^+) sulfate; oxo(sulfato)vanadium; oxovanadium(IV) sulfate; vanadium oxide sulfate; vanadium oxosulfate; vanadium oxysulfate; vanadium sulfate; vanadic sulfate; vanadyl monosulfate; vanadin(IV) oxide sulfate	Sodium vanadate; sodium trioxidovanadate(1^-); sodium vanadium oxide; sodium vanadium trioxide; vanadic acid, monosodium salt; sodium vanadate(V)	Ammonium trioxovanadate(1^-); ammonium tris(oxido)vanadate(1^-); ammonium monovanadate; ammonium vanadate(V); vanadic acid, ammonium salt; ammonium vanadium oxide; ammonium vanadium trioxide	Trisodium tetraoxidovanadate(3^-); sodium vanadium oxide, trisodium vanadate, sodium vanadate(V), vanadic acid, trisodium salt	Vanadium oxide; mu-oxido[tetrakis(oxido)]divanadium; divanadium pentoxide; vanadic anhydride; vanadin(V) oxide; vanadium(V) oxide
Water solubility (mol/L)[b]	--	--	--	--	--	--

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Reaction: Hydrolysis of vanadium solids

Compounds:
Vanadium salts

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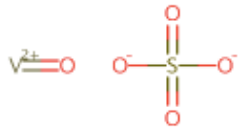
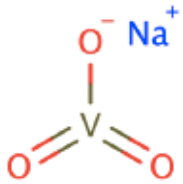
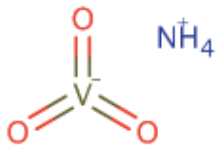
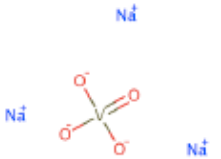
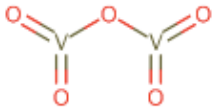
Structure						

First reaction discussed – reaction with water: Hydrolysis (pH dependent)

Specific Reactions:

$VOSO_4 + 5H_2O \rightarrow \mathbf{VO(H_2O)_5^{2+}} + SO_4^{2-}$ (pH is acidic)

$NaVO_3 + H_2O \rightarrow \mathbf{H_2VO_4^-} + Na^+$ (pH near 7)

$Na_3VO_4 + 2H_2O \rightarrow \mathbf{H_2VO_4^-} + 3\ Na^+ + 2OH^-$ (pH is basic)

$V_2O_5 + H_2O + 2\ NaOH \rightarrow \mathbf{2H_2VO_4^-} + 2\ Na^+$ (pH is acidic)

Language needs to properly reflect species that exists

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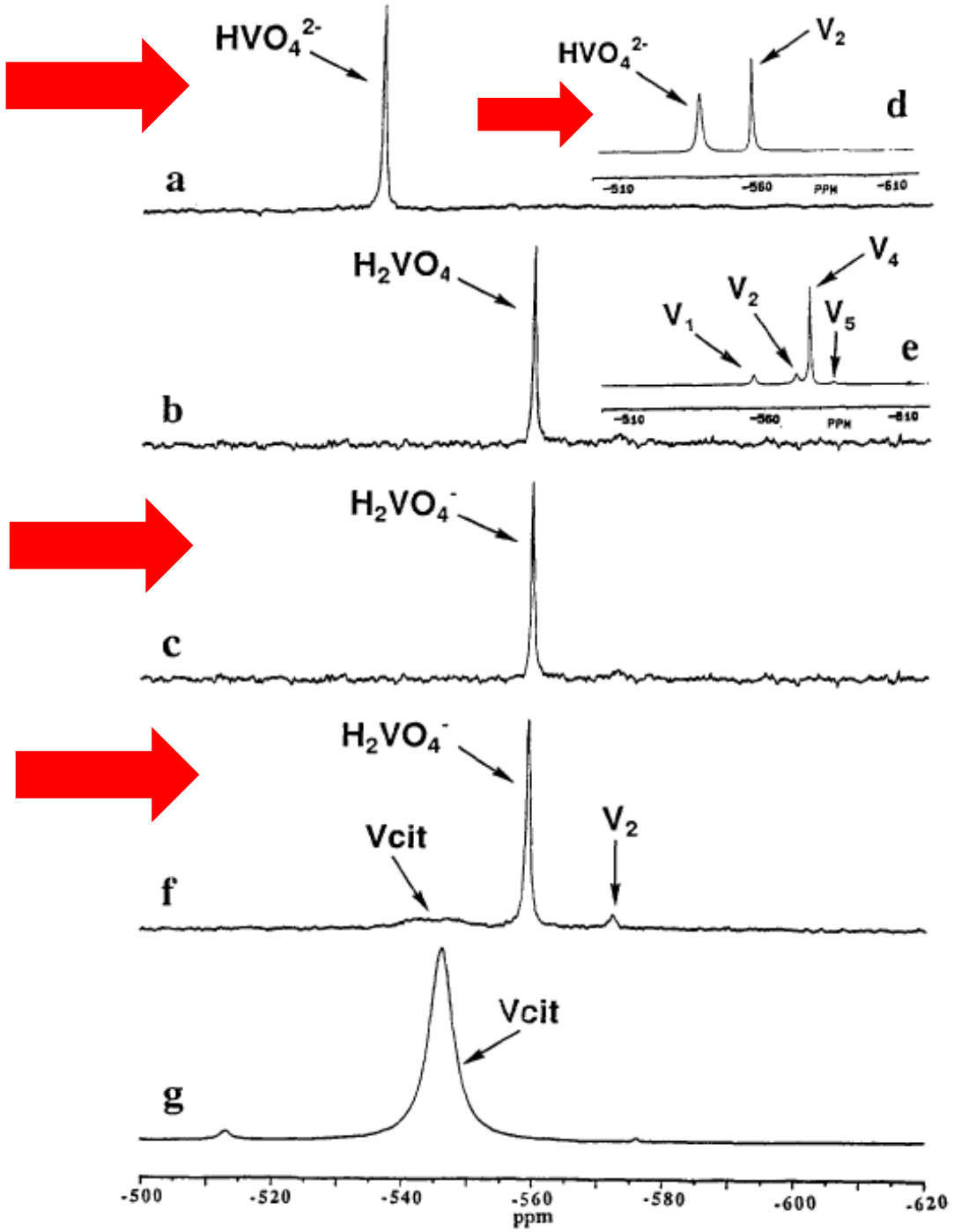
Comparing $NaVO_3$ and Na_3VO_4

^{51}V NMR spectra of vanadate solutions prepared $NaVO_3$ and Na_3VO_4:

a) 0.38 mM vanadate prepared from Na_3VO_4 (pH 10.50),
b) 0.38 mM vanadate prepared from $NaVO_3$ (pH 7.04),
c) 0.4 mM vanadate prepared from Na_3VO_4 and adjusted to pH 7.04,
d) 10.0 mM vanadate prepared from Na_3VO_4 (pH 12.5),
e) 10.0 mM vanadate prepared from $NaVO_3$ (pH 7.04),
f) 0.38 mM Na_3VO_4 adjusted to pH 7.04 with citric acid,
g) 10.0 mM $NaVO_3$ and 40.0 mM citrate at pH 7.04.



Crans et al. *Cell Mol. Biochemistry*, **1995**, 17-24.

IRIS Program Public Science Meeting Aug. 19, 3-5 pm EST

Acid-Base & Oligomerization Reactions

Vanadium in oxidation state V

$VO_4^{3-} + H_2O \rightarrow HVO_4^{2-} + HO^-$

$HVO_4^{2-} + H_2O \rightarrow H_2VO_4^- + HO^-$

$H_2VO_4^- + H_3O^+ \rightarrow H_3VO_4 + H_2O$

$(H_3VO_4 \rightarrow H_2O + VO_2^+ + HO^-)$

Vanadium in oxidation state IV

$VO(H_2O)_5^{2+} + SO_4^{2-} \rightarrow VO(OH)(H_2O)_5^{2+} + HSO_4^-$

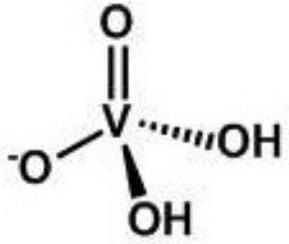
Condensation Reactions

(abbreviate V_1, V_2, V_4, V_5 , V_{10})

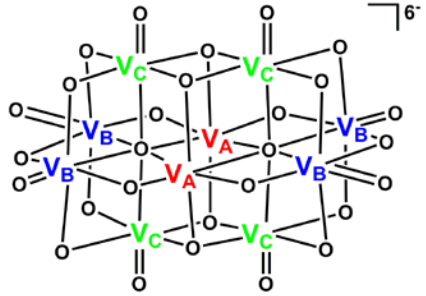
$V_1 + V_1 \rightarrow V_2$

$\rightarrow V_4$

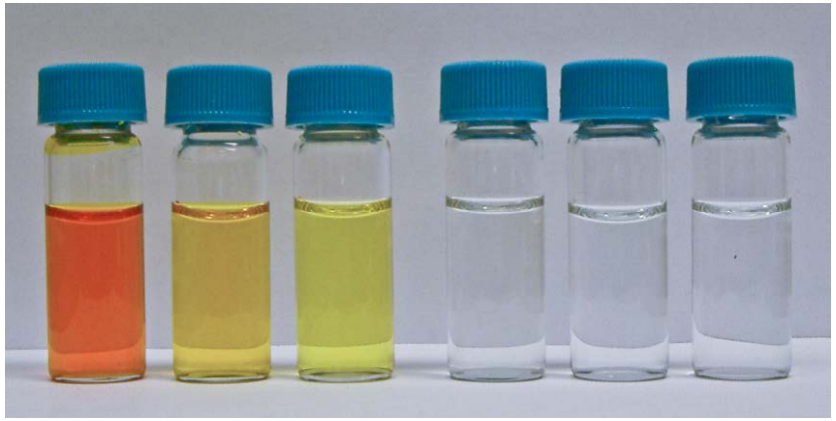
$\rightarrow V_{10}$



Vanadate and decavanadate



From the left the three metavanadate solutions (pH 7.3-7.8) at 0.005, 0.05, 0.5 M



From the right three decavanadate solutions (pH 5.8-6.0) at 0.005, 0.05, 0.5 M

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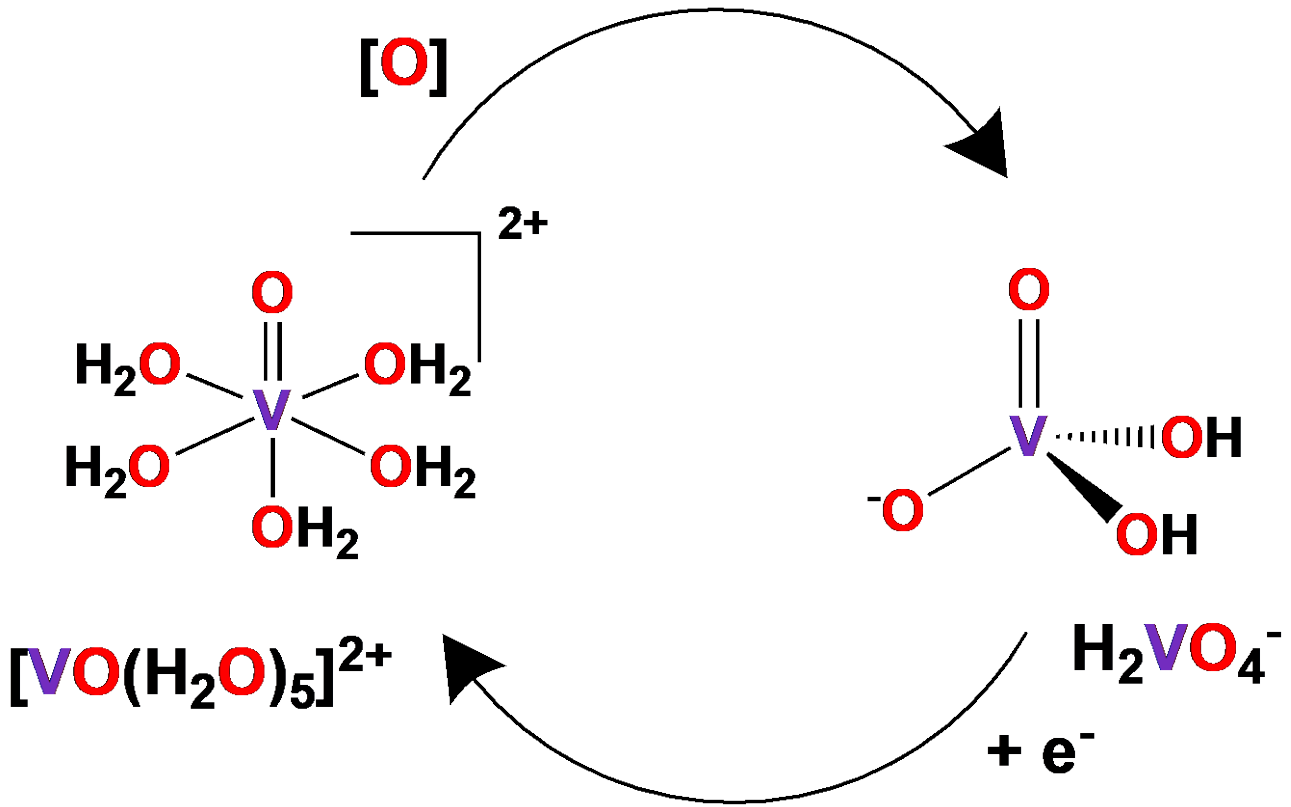
Redox chemistry of vanadium salts

Redox reactions occur at the suitable redox potential which varies with pH and other reaction conditions.

A **cycling between Vanadium(V) and Vanadium(IV)** occur under physiological conditions

Importantly, all these reactions (hydrolysis, acid/base, condensation and redox) take place at the same time



Crans et al. *Chem. Rev.* 2004, 104, 849-902

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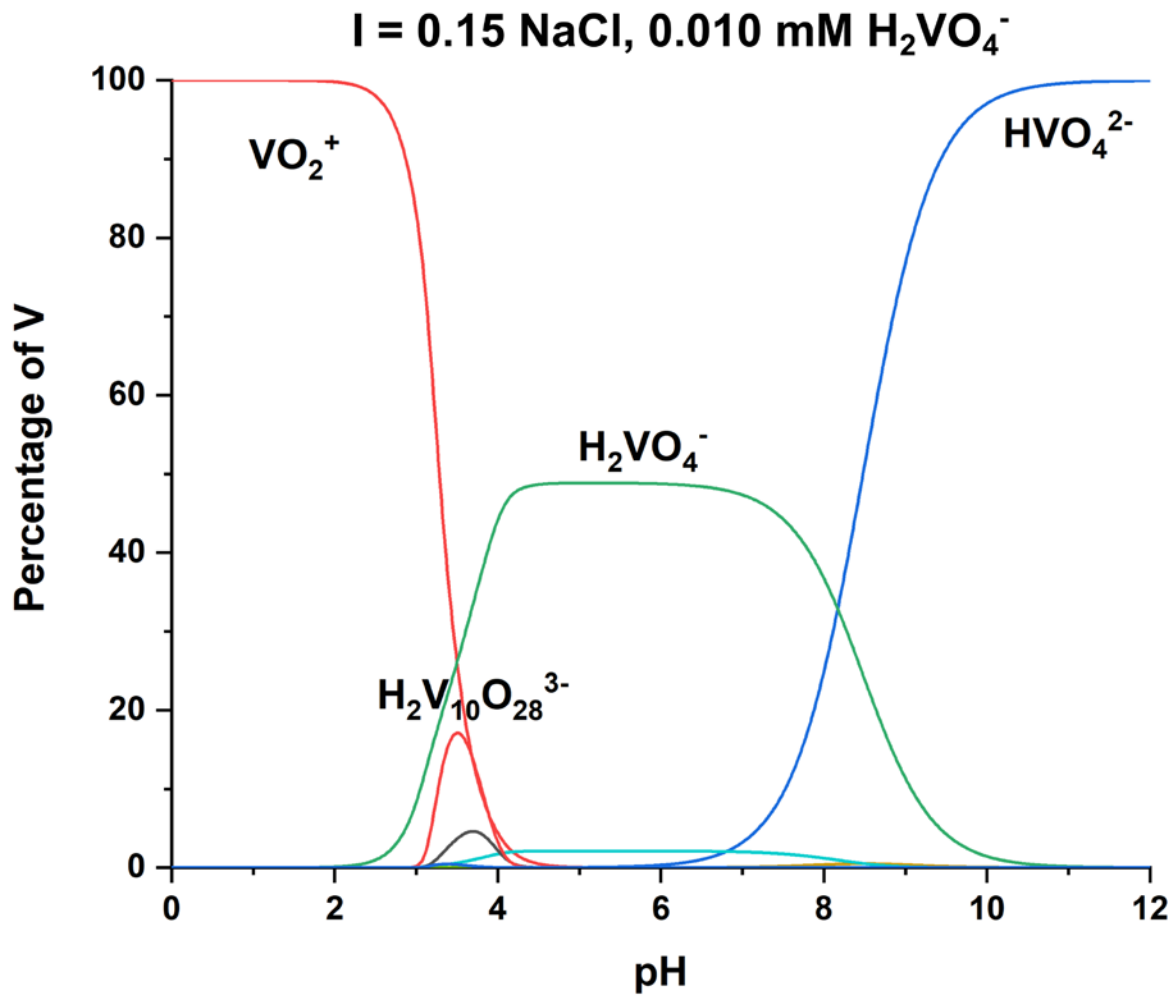
Distribution Diagrams V(V) - at physiological levels



At low concentration speciation is simple and mainly mononuclear species present

Crans et al. "Metal Toxicology Handbook" 2020
Bagchi D. and Bagchi M. in press

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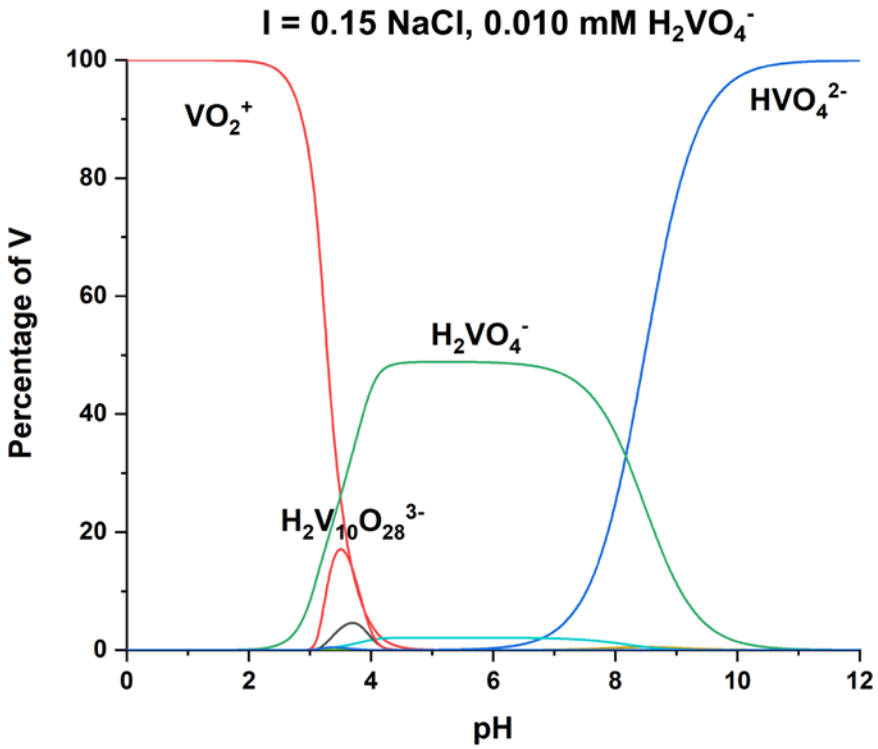
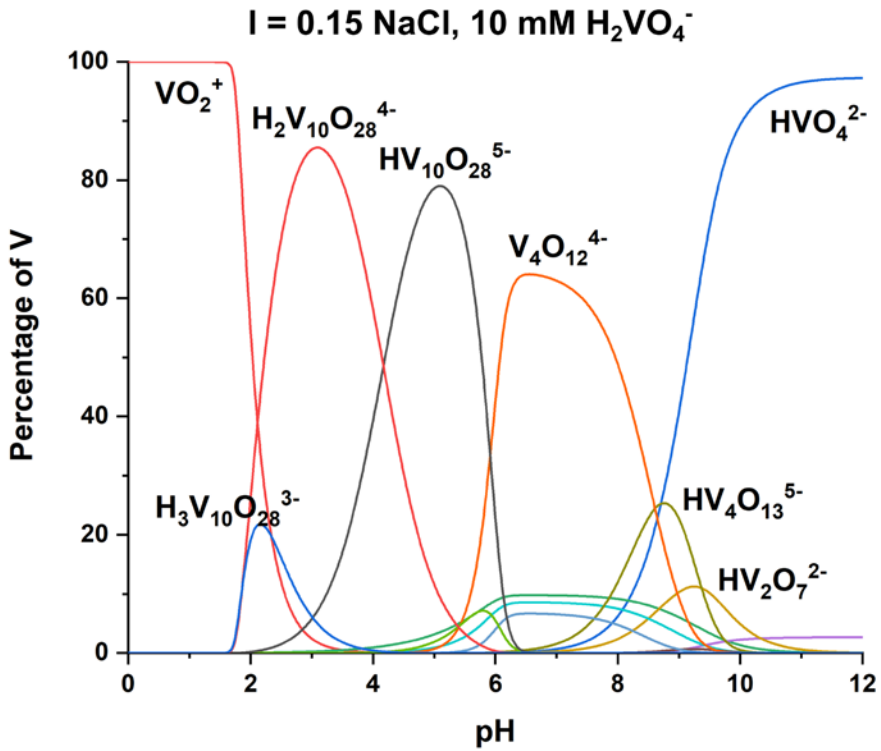
Distribution Diagrams V(V) – low and higher concentrations





At higher concentrations other species form – and are present when researchers are preparing experiments

Important to recognize that equilibrium may not be rapid

Crans et al. "Metal Toxicology Handbook" 2020 Bagchi D. and Bagchi M. in press

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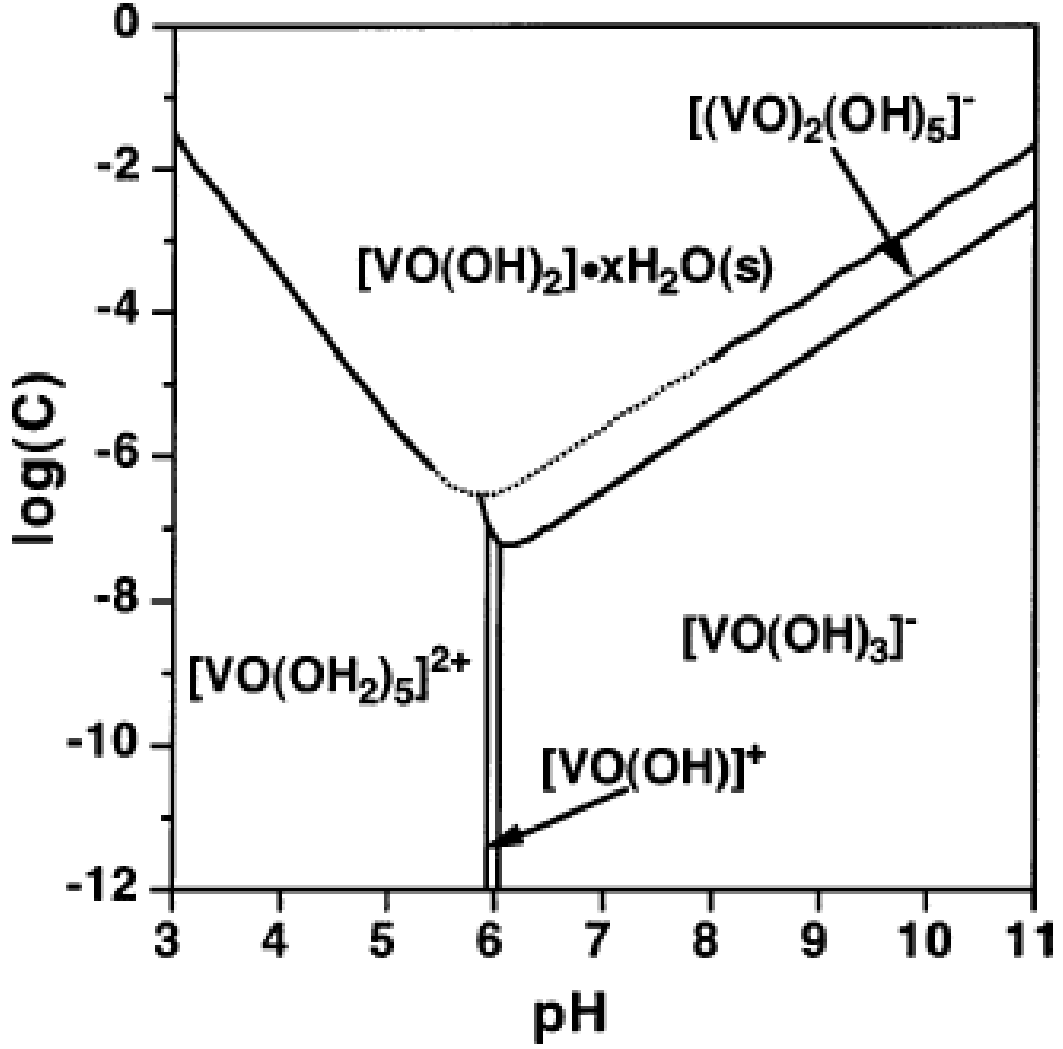
Distribution Diagrams V(IV)



Formation of $VO(OH)_2$ and derived species that are EPR silent complicate investigations near neutral pH

Below 1 microM except between pH 6-7 speciation is $VO(OH_2)_5^{2+}$ $[(VO)_2(OH)_5]^-$, and $[VO(OH)_3]^-$

Crans et al. *Chem. Rev.* 2004, 104, 849-902

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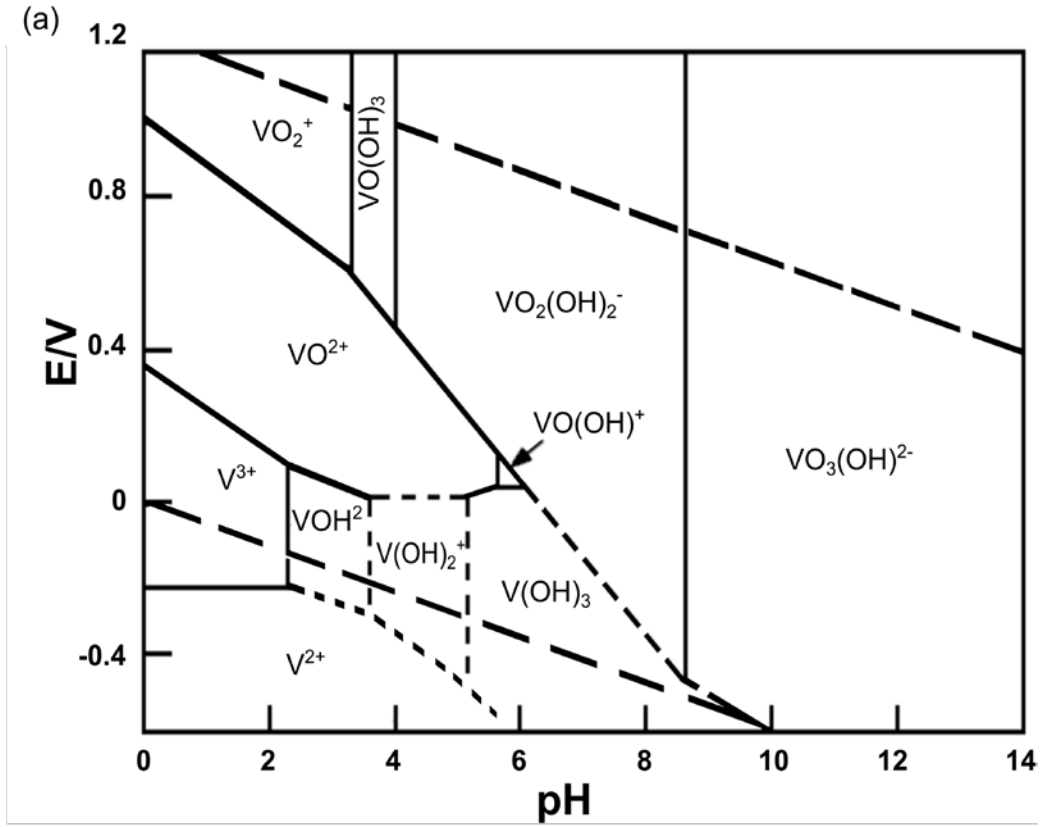
Distribution Diagrams; at physiological levels



Representation of the Pourbaix diagram of vanadium of ionic strength of (a) 10^{-6} M
Crans et al. *Chem. Rev.* 2004, 104, 849-902

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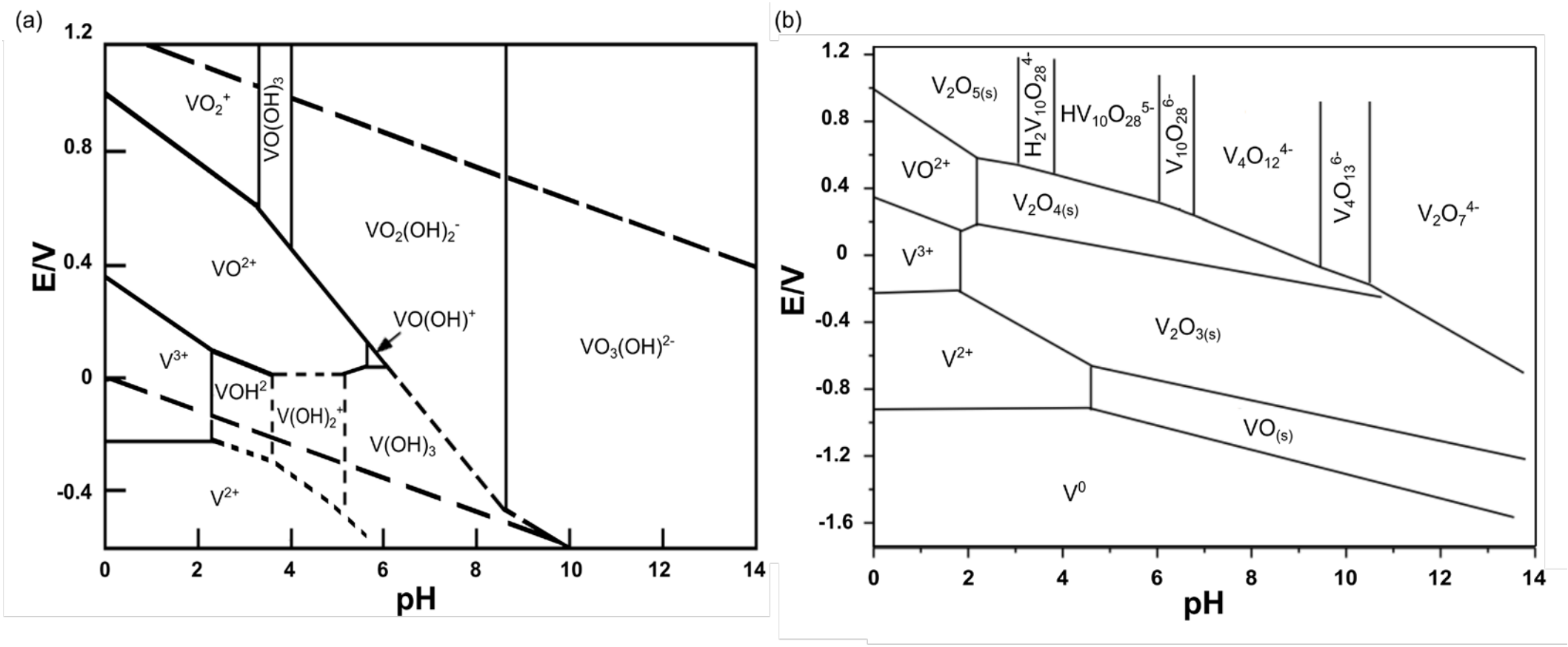
Pourbaix Diagrams; low and higher concentrations



Representation of the Pourbaix diagram of vanadium of ionic strength of (a) 10^{-6} M (1) and (b) 1 M at 25°C (2)
(1) Crans et al. *Chem. Rev.* 2004, 104, 849-902; (2) Povar et al. J. Electrochem. Sci. Eng. 2019, 9, 75–84.

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Biological effects as a consequence of speciation

Chemical Speciation (slides 1-15)

- **Illustrate and define speciation**
- **Fundamental chemical and physical properties**
- **Speciation profile and Pourbaux diagrams**

Biological effects of speciation (slides 16-19)

- **Speciation cause different biological effects**

[a] **Differences in uptake by vanadium(V) and vanadium(IV)**

Future and recommendations with measurements (slides 20-21)

- **Methods to measure V-content and speciation**

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Inhibition by different V-compounds and salts: Sarcoplasmic Reticulum Calcium ATPase

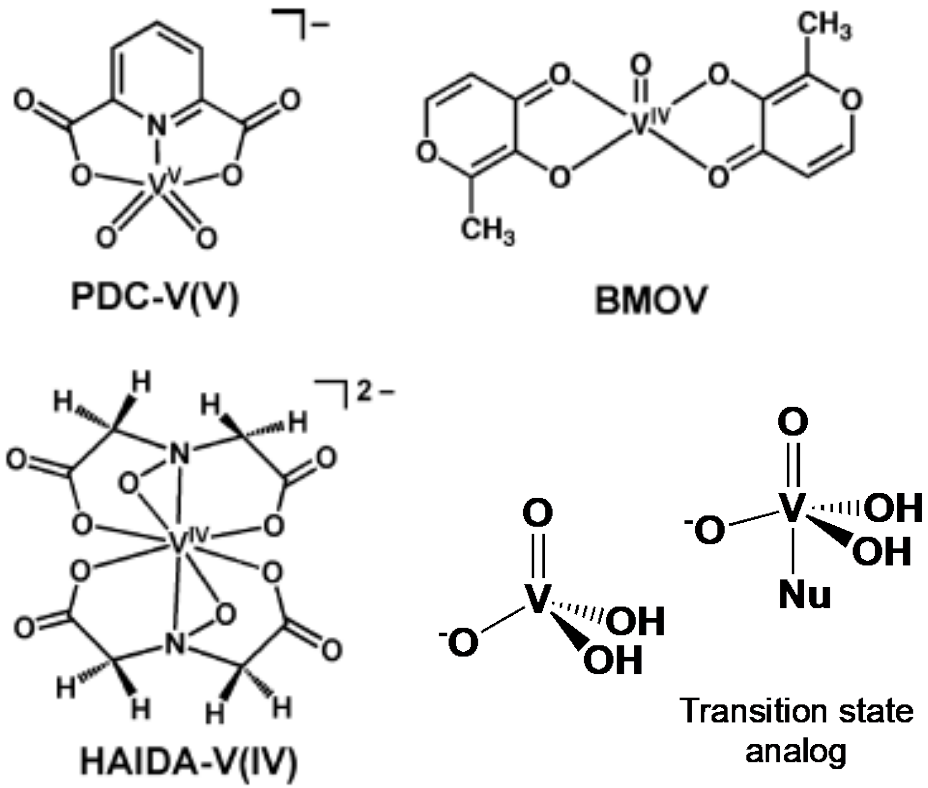
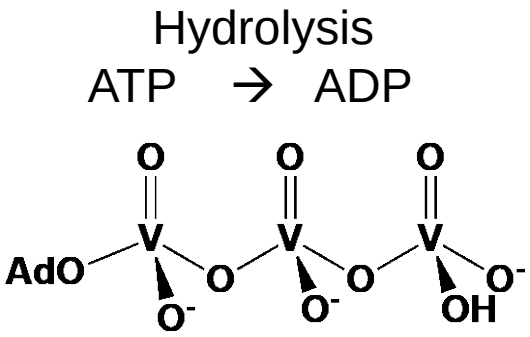
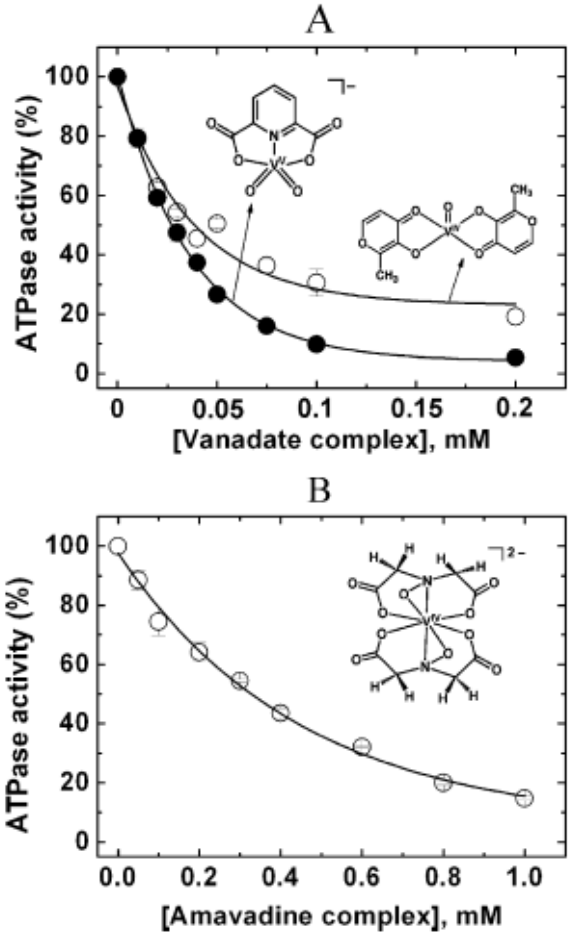


Figure 1. Molecular structures of PDC−V(V), BMOV, HAIDA−V(IV),



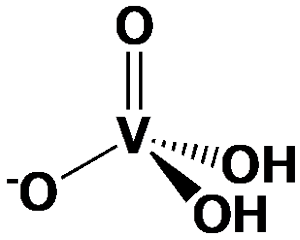
The Sarcoplasmic Reticulum Ca^{2+}-ATPase was inhibited by all three of these complexes – the order was **PDC-V(V) > BMOV > vanadate > HAIDA-V(IV)**, and the IC_{50} values were **25, 40, 80, and 325** µM,

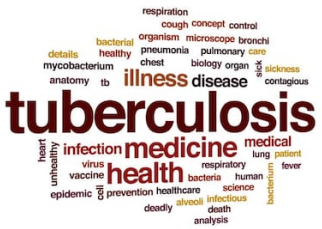
Different species - different activity



Aureliano et al. *Inorg. Chem.,* **2008,** *47,* 5677-5684

V_1 affects growth less than V_{10} on *Mycobacteria*





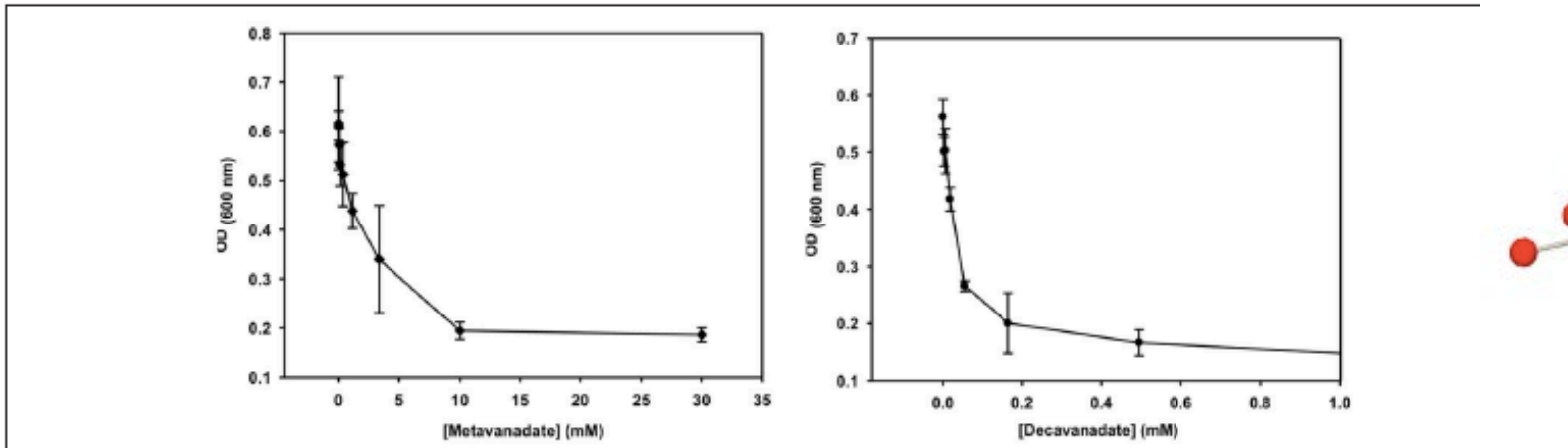


FIGURE 4 | The growth curve is shown for treatment with vanadate (left, prepared from a 40 mM colorless metavanadate solution) and decavanadate [right, prepared from a 100 mM orange decavanadate solution (1.0 M V-atoms) on *M. tb*].

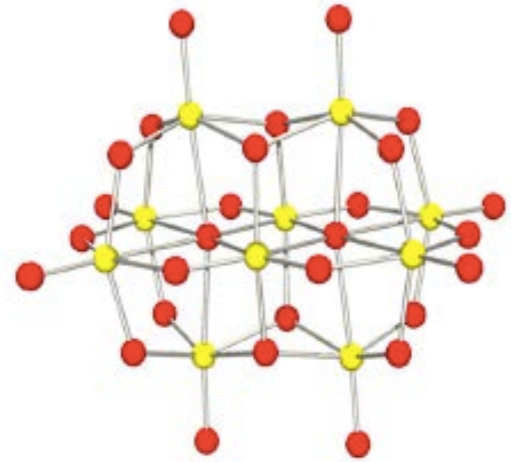


TABLE 2 | The EC_{50} values for V_1 and V_{10} treated *Mycobacterium tuberculosis* and *smegmatis*.

	EC_{50} (*M. tb*) (mM)	Stand. error	EC_{50} (*M. tb*) (mM V-atoms)	Stand. error	EC_{50} (*M. smeg*) (mM)	Stand. error	EC_{50} (*M. smeg*) (mM V-atoms)	Stand. error
V_1	2.0	0.43	2.0	0.43	0.19	0.071	0.19	0.071
V_{10}	0.029	0.005	0.29	0.05	0.0037	0.0004	0.037	0.004

Different species - different activity

Samart et al. *Frontiers in Chemistry*, **2018,** 6, article #519 (16p).

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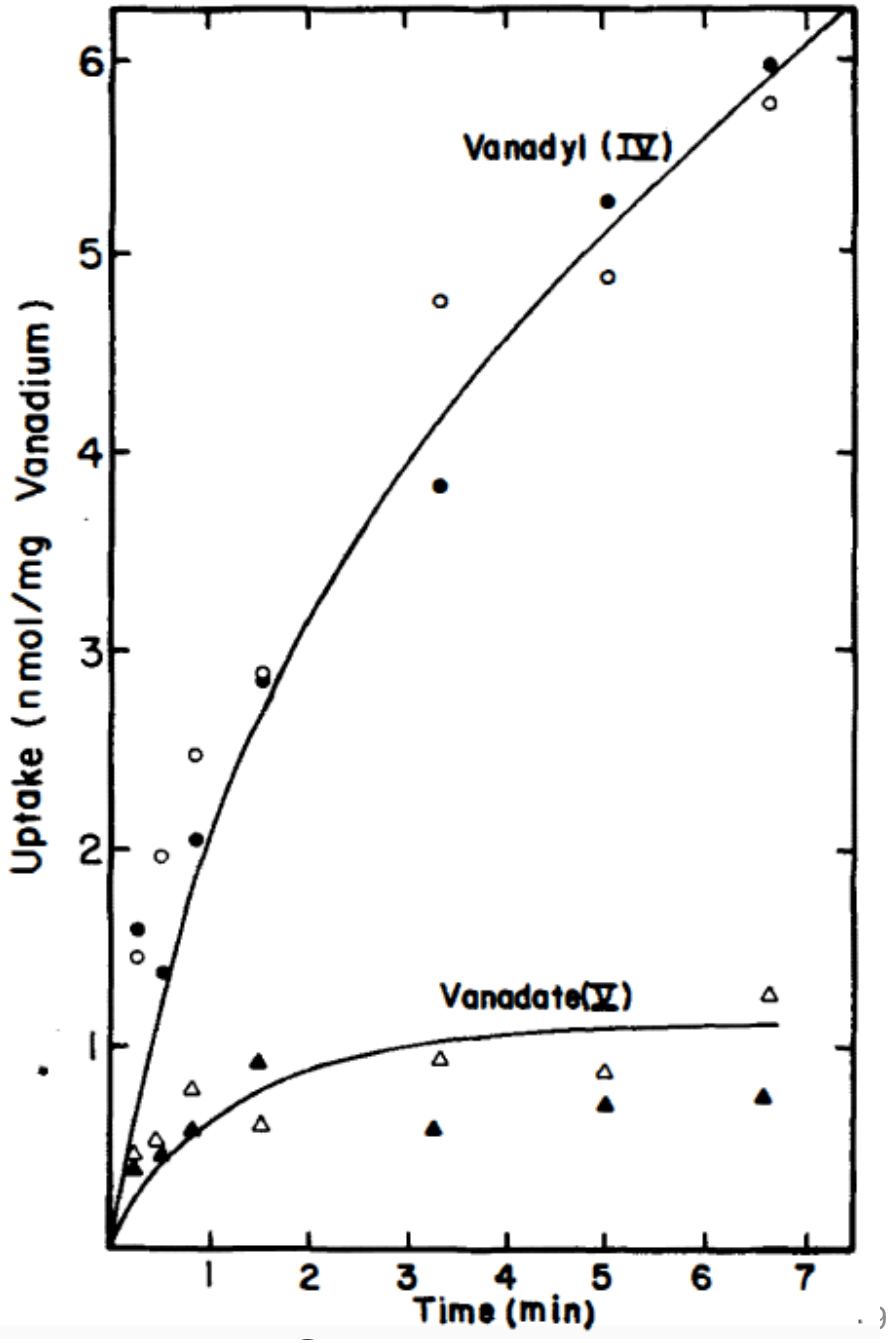
Cellular uptake difference between vanadyl (V(IV)) and vanadate (V(V))

Cellular accumulation of vanadate and vanadyl. Cell growth and uptake studies were done using radiolabeled vanadium compounds. o represent 200 µM [^{48}V]vanadyl uptake and • represent 200 µM [^{48}V]vanadate uptake.



Willsky et al. *J. Biol. Chem.* **1984**, *259*, 13273-13281

Measuring vanadium and speciation

Chemistry section (slides 1-15)
- Illustrate and define speciation
- Fundamental chemical and physical properties
- Speciation profile and Pourbaux diagrams

Biological effects (slides 16-19)
- Speciation cause different biological effects
- [a] Differences in uptake by vanadium(V) and vanadium(IV)

Future and recommendations with measurements (slides 20-21)
- **Methods to measure V-content and speciation**

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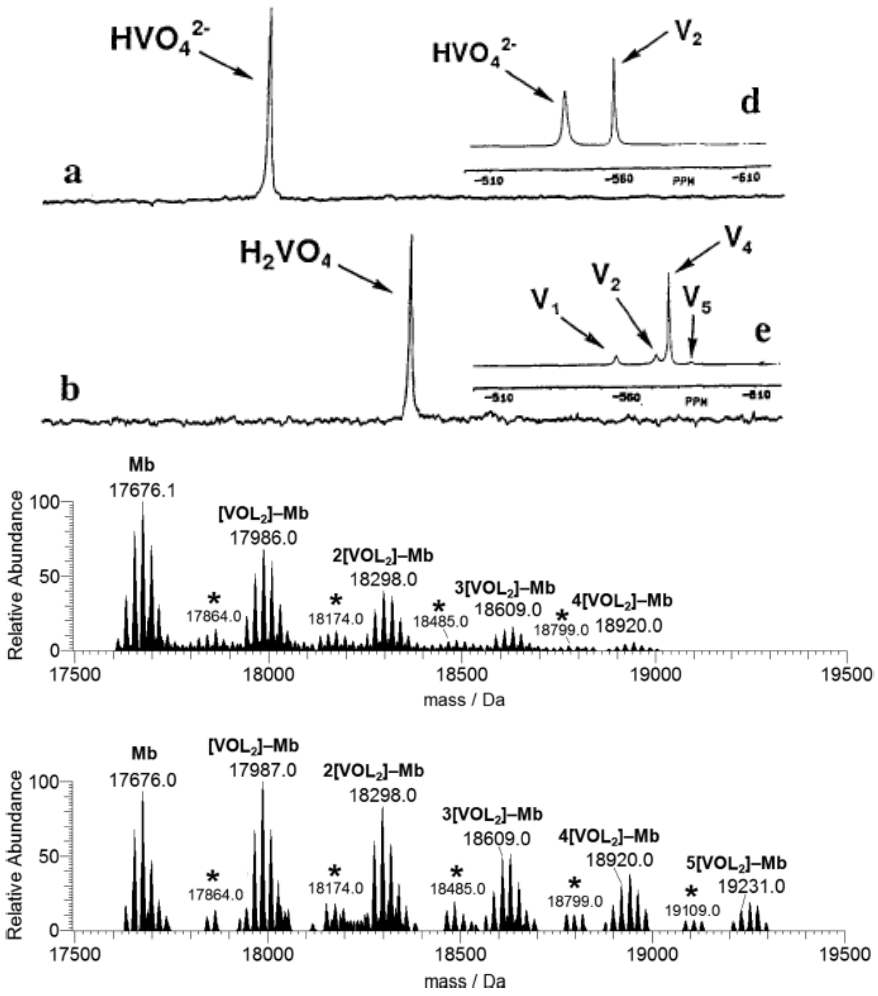
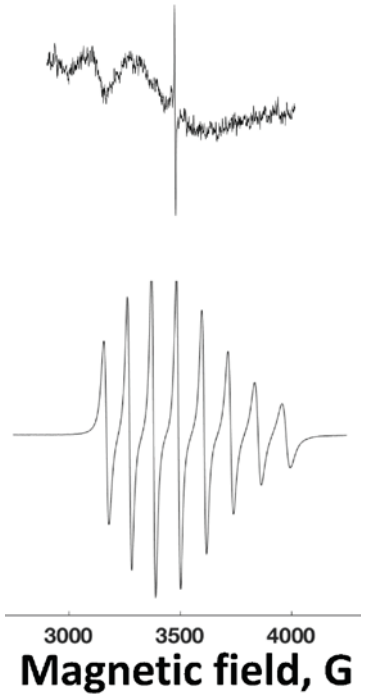
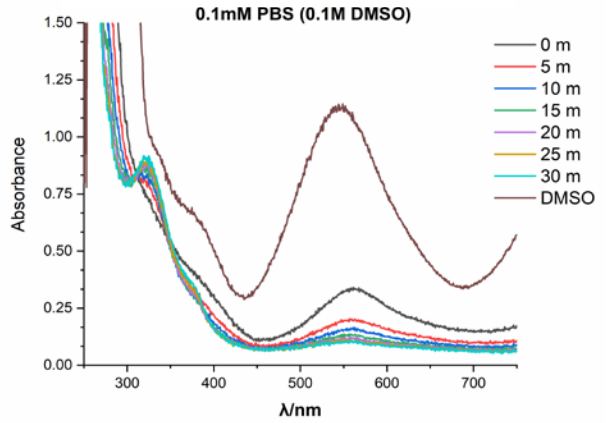
Measuring vanadium levels



Total vanadium
Atomic absorbance spectroscopy
Inductively coupled plasma
Various mass spectroscopies
X-ray absorbance spectroscopy

Specific oxidation states
Vanadium(V)
Magnetic resonance (NMR)
UV-vis and IR spectroscopy
Vanadium(IV)
Magnetic resonance (X-band EPR)
UV-vis and IR spectroscopy
Vanadium(III)
Magnetic resonance (High field EPR_
UV-vis and IR spectroscopy





Ugone et al *Inor. Chem.* 2020,59, 9739-9755

IRIS Program Public Science Meeting Aug. 19, 3-5 pm EST

Debbie.Crans@ColoState.edu

Topic: Consideration of vanadium speciation.

By Debbie C. Crans; Colorado State University

Chemical Speciation (slides 1-15)

- **Illustrate and define visible speciation**
- **Fundamental chemical and physical properties**
- **Speciation profile and Pourbaux diagrams**

Biological effects of speciation (slides 16-19)

- **Speciation cause different biological effects**
- **[a] Differences in uptake by vanadium(V) and vanadium(IV)**

Future and recommendations with measurements (slides 20-21)

- **Methods to measure V-content and speciation**

Recommendations for developing *the PECO criteria for studies and setting guidelines for safe limits in drinking water*

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