

# Vanadium detoxification: On the interaction of oxovanadium(IV) and other vanadium species with 2,3-dimercapto-1-propanesulfonate

Patricia A.M. Williams, Enrique J. Baran\*

*Centro de Química Inorgánica (CEQUINOR/CONICET, UNLP), Facultad de Ciencias Exactas, Universidad Nacional de La Plata, C. Correo 962, 1900 La Plata, Argentina*

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## Abstract

The interaction of the  $\text{VO}^{2+}$  cation with the sodium salt of 2,3-dimercapto-1-propanesulfonic acid (DMPS) was investigated by electron absorption spectroscopy in aqueous solution, in the pH range between 4 and 12. The spectral behavior points to the generation of a  $[\text{VO}(\text{DMPS})_2]^{4-}$  complex in which the oxocation interacts with two pairs of deprotonated  $-\text{SH}$  groups of the ligand. By spectrophotometric monitoring it was found that DMPS rapidly reduces vanadates(V) to  $\text{VO}^{2+}$  which may be chelated by an excess of the acid. DMPS produces also the slow reduction of a  $\text{V}_2\text{O}_5$  suspension at pH 7.1. The results of this study suggest that DMPS may be a potentially useful detoxification agent for vanadium.

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Environmental contamination by vanadium has dramatically increased during the last years due to the widespread use of fossil fuels, many of which liberate finely particulate vanadium pentoxide to the atmosphere during combustion [1–3]. Therefore, and also owing to the emerging interest in the pharmacological effects of some of its compounds [4], the toxicology and detoxification of vanadium constitute areas of increasing interest.

Vanadium toxicity has been reported in experimental animals and in humans. The degree of toxicity depends on the route of incorporation, valence, and chemical form of the element and is also, to some extent, species-dependent. In general it increases as valence increases, pentavalent vanadium being the most toxic. Although under natural conditions toxic effects do not occur frequently, at high doses or as a consequence of chronic exposure it is a relatively toxic element for humans [5].

The upper respiratory tract is the main target in occupational exposure. Acute and chronic exposure gives rise to

conjunctivitis, rhinitis, and asthma-like diseases in more severe cases. It can also produce fatigue, cardiac palpitation, gastrointestinal distress, and kidney damage. In human, acute toxicity has been observed in vanadium miners and industrial workers exposed to high doses of vanadium. The classic symptoms of this malady, referred to as “green tongue” syndrome, are a green coloration of the tongue, accompanied by some of the above-mentioned disorders [5].

Chelation therapy occupies a central place in modern medicine and pharmacology as extensive clinical experience and continuous studies with laboratory animals demonstrate that acute or chronic human intoxications with a variety of metals can be considerably improved by administration of a suitable chelating agent [6–10].

In recent years two new and very promising chelating agents have been introduced into the medical praxis, they are *meso*-2,3-dimercaptosuccinic acid (DMSA) and 2,3-dimercapto-1-propanesulfonic acid (DMPS) [7,8,11,12]. Both drugs, which are very stable and show low toxicity and side effects, are available as tablets for oral administration [7,11–16].

\* Corresponding author. Tel./fax: +54 221 4259485.

E-mail address: [baran@quimica.unlp.edu.ar](mailto:baran@quimica.unlp.edu.ar) (E.J. Baran).

Recent advances in a better knowledge of vanadium metabolism in the higher forms of life [17,18] allow a better understanding of the biological detoxification processes and the development of new detoxification agents for this element [5]. In a previous paper we have shown that DMSA may be a potentially useful detoxification agent for vanadium [19]. In this paper we present the results of our studies of the interaction of oxovanadium(IV) and some other vanadium species with DMPS (Fig. 1).

The sodium salt of 2,3-dimercapto-1-propanesulfonic acid from MP-Biochemicals,  $\text{NaVO}_3$  from Aldrich, and  $\text{VOCl}_2$  (50% solution) from Carlo Erba was used as supplied. Pure and finely divided  $\text{V}_2\text{O}_5$  was obtained by carefully heating of  $\text{NH}_4\text{VO}_3$  (Carlo Erba) up to  $450^\circ\text{C}$  in a muffle furnace in air [20]. All the other reagents were analytical grade.

All the experiments were performed under a nitrogen atmosphere to avoid oxidation phenomena. The electronic absorption spectra were measured with a Hewlett–Packard 8452 diode-array spectrophotometer, using 10-mm quartz cells.

Metal and ligand solutions were mixed in different stoichiometric relations and the desired pH values were adjusted either with diluted HCl or NaOH solutions.

It is well known that molecules containing thiol groups such as L-cysteine [21], reduced glutathione [17,22], or dithiothreitol [23] are efficient reducing agents for vanadium(V), when used in excess, and this was also confirmed recently for DMSA [19]. Preliminary qualitative experiments clearly showed that also DMPS is able to reduce vanadium(V) to vanadium(IV). Therefore, we have first investigated the characteristics of the interaction of the reduced species (oxovanadium(IV),  $\text{VO}^{2+}$ ) with DMPS to attain an insight into the form in which this species can be stabilized by an excess of the reducing ligand.

DMPS (1 mM) was dissolved in 10 mL of distilled water, generating a solution with pH 4.4. After addition of 0.5 mM of  $\text{VOCl}_2$  solution the pH drops to 2.9 and a transparent greenish solution is obtained. After raising the pH-values by NaOH addition, precipitation of a solid product is observed up to pH 12. Acidification of the solution containing the suspended solid causes its redissolution at pH 2 but the generated greenish solution shows an electronic absorption spectrum which closely resembles that of  $[\text{VO}(\text{H}_2\text{O})_5]^{2+}$  [24,25], indicating that the cation remains uncomplexed.

In second series of experiments an excess of ligand were used, employing 10:1 ligand to metal ratios. In these experiments 1 mM DMPS, dissolved in 10 mL of water were reacted with 0.1 mM  $\text{VOCl}_2$ . Working with these ligand

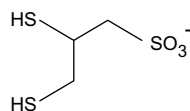


Fig. 1. Schematic structure of the DMPS anion.

to metal ratios the solutions remained transparent in the full pH-range between 4.0 and 12.0, without any signs of hydrolytic phenomena. The obtained solutions show a characteristic electronic absorption spectrum (Fig. 2) with a single maximum at 628 nm ( $\epsilon = \text{ca. } 75 \text{ M}^{-1} \text{ cm}^{-1}$ ), which intensity remains constant at  $\text{pH} \geq 7.2$ . The second expected transition, which is usually weaker, could not be identified, probably due to the very strong increase of the absorption below 550 nm. It must be remembered that oxovanadium(IV) species exhibits a characteristic three-band spectrum in which the higher energy band is usually masked by a charge transfer absorption [25]. In the present case, this charge transfer is especially strong, overlapping the two highest energy d–d transitions.

The position of the observed electronic transition band is comparable to that found in the  $\text{VO}^{2+}$ /DMSA system [19] as well as in the complexes which oxovanadium(IV) generates with dithiothreitol [26] and with a series of bis(*N,N*-disubstituted) dithiocarbamates [27]. In all these cases  $\text{VO}_2$  species are generated and coordination takes place through two pairs of deprotonated –SH groups [19,26,27]. Therefore, one may expect a totally similar situation in the present case, admitting the formation of a  $[\text{VO}(\text{DMPS})_2]^{4-}$  complex.

To verify the reducing action of DMPS over vanadium(V) species, we have also investigated its interaction with  $\text{NaVO}_3$  (an aqueous solution of which contains a mixture of different vanadate(V) species in equilibrium, depending of the pH-value and the vanadium concentration [28]) and  $\text{V}_2\text{O}_5$ . For the experiments with vanadate a 100:1 DMPS/ $\text{NaVO}_3$  ratio (1 mM DMPS and 0.01 mM  $\text{NaVO}_3$ , in 10 mL of water) were used. Rapid

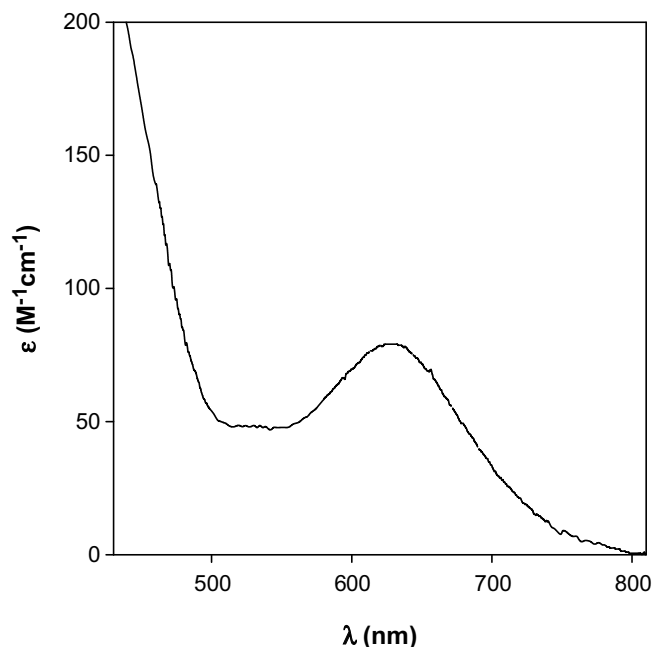


Fig. 2. Electronic absorption spectrum of an aqueous solution of DMPS: $\text{VO}^{2+}$  at a 10:1 ratio (pH 7.2) under a  $\text{N}_2$  atmosphere.

reaction is observed even at the initial pH of the obtained solution (pH 4.2). In the pH range between 7.2 and 12.0, the spectra recorded with the generated solutions are totally similar to that shown in Fig. 2, confirming the for-

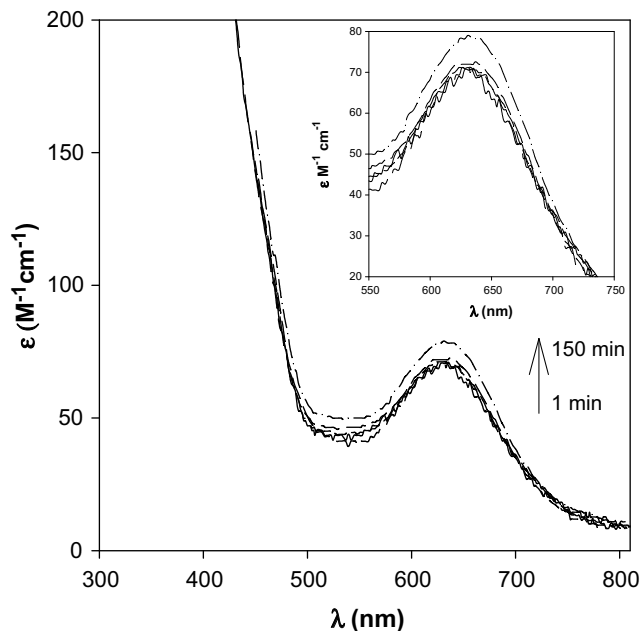


Fig. 3. Electronic absorption spectra of an aqueous solution of DMPS:VO<sup>2+</sup> (obtained after reduction of VO<sub>3</sub><sup>-</sup>) at a 100:1 ratio (pH 7.5) under a N<sub>2</sub> atmosphere, measured at different times after mixing the reagents (1, 25, 60, 100, and 150 min). The inset allows a better insight onto the absorption maxima.

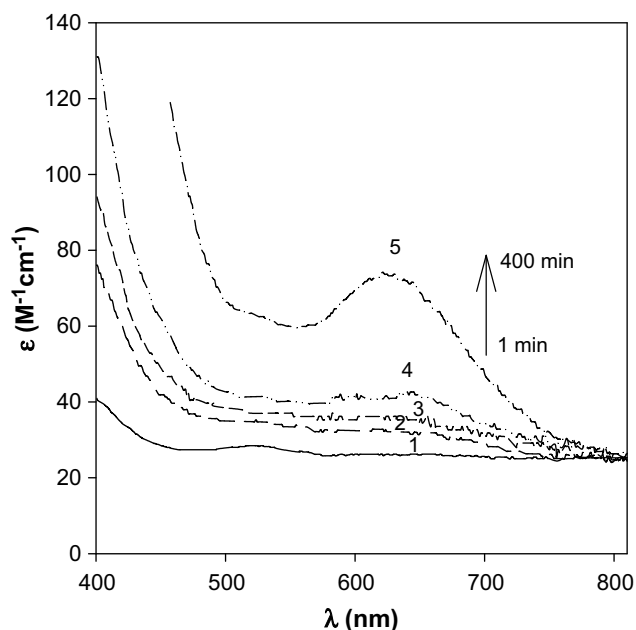


Fig. 4. Electronic absorption spectra of a suspension of 0.005 mM of V<sub>2</sub>O<sub>5</sub> mixed with 1 mM of DMPS in water (pH 7.1) under a N<sub>2</sub> atmosphere, measured at different times after mixing (1: 5 min; 2: 15 min; 3: 30 min; 4: 75 min; 5: 400 min).

mation of the same [VO(DMPS)<sub>2</sub>]<sup>4-</sup> species described in the previous section.

In Fig. 3 a typical reduction experiment performed at pH 7.2 is shown proving the very rapid transformation of vanadium(V) to VO<sup>2+</sup>.

In the case of vanadium pentoxide, a suspension of 0.005 mM V<sub>2</sub>O<sub>5</sub> in 10 mL of water was mixed with 1 mM DMPS and the pH adjusted to 7.1. As shown in Fig. 4, this reaction is extremely slow in comparison to the previous one. This can surely be ascribed to the heterogeneous nature of the reaction in this case, in which one of the partners (V<sub>2</sub>O<sub>5</sub>) is present in the form of a finely divided solid suspension. Notwithstanding, spectrophotometric monitoring of the reaction showed an increment of absorbance with time and after about 6 h a spectral pattern similar to that shown in Fig. 2 can be observed, which becomes even better defined at longer reaction times.

The obtained results clearly show that DMPS appears as a new very promising and interesting detoxification agent for vanadium(V), which merits to be further explored, for example, with laboratory animals as a next step.

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