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Voltammetric and Spectroscopic Studies of Vanadium(V)– Nicotinamide Interactions at Physiological pH

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The interaction of nicotinamide (NA) with NH_4VO_3 at the physiological pH (pH 7.4) was studied by voltammetry and UV-Vis spectroscopy. The reduction of V(V) ions complexed with NA in phosphate buffer (pH 7.4) was observed as a well-defined reversible reduction peak at –0.35 V. The stoichiometric (metal:ligand) ratio of the complex of V(V) with NA was determined as 1:2 by the mole ratio method.

Key Words: Vanadium complexes, nicotinamide, voltammetry, spectroscopy.

Introduction

Vanadium is a trace transition metal with relevant biological properties.[1] In recent years there has been extensive interest in the chemistry of oxovanadium complexes. Complexes of vanadium are very interesting as model compounds to clarify several biochemical processes.[2–4] Some complexes of V(IV) and V(V) have shown insulin-mimetic actions.[4–6] In rodent models of obesity and type 2 diabetes mellitus, vanadium improves glucose metabolism by restoring both hepatic and skeletal muscle insulin sensitivity.[7,8] An important physiological role of vanadate is inhibition of some ATPases.[9,10] The oxidation mechanisms of biologically important substances by vanadium(V) have been studied in detail because of their relevance in bioinorganic chemistry.[11–13]

Nicotinamide (NA) (Scheme) is a derivative of niacin (vitamin B_3). Pharmacological doses of NA are being studied for their potential benefit in the prevention[14] and treatment[15] of diabetes. NA can protect vital pancreatic cells from diabetes-inducing factors;[16] however, NA appears to have been eliminated as a substance to halt the onset of type 1 diabetes.[17]

Although the synthesis, characterization, and electrochemical behavior of complexes of NA with some metal ions (Cu(II),Co(II),Ni(II), Fe(II), Mn(II), and Zn(II)) were reported,[18–20] we were not able to find

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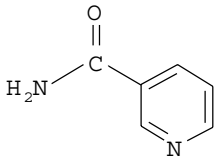
any references to the interaction mechanism of NA with NH_4VO_3 in solution in the chemical literature. The present paper deals with the interaction of NH_4VO_3 with NA at physiological pH. This interaction was studied by UV-Vis spectroscopy, cyclic voltammetry (CV), and square-wave voltammetry (SWV) techniques. Voltammetric measurements of this interaction seemed to provide a better understanding of the biochemistry and redox chemistry of vanadium.



Scheme. The molecular structure of NA.

Experimental

Apparatus

Voltammetric measurements were performed using an EG & G PAR 384B polarographic analyzer connected to an EG & G PARC 303A polarographic stand (Princeton, NJ, USA). A hanging mercury drop electrode (HMDE), an Ag|AgCl|KCl_{sat} reference electrode, and a Pt wire auxiliary electrode were used. Voltammograms were recorded with a Houston Instrument DMP-40 plotter (Austin, TX, USA).

The electronic absorption spectra in the 800-200-nm range were recorded on a Unicam V2-100 UV-Vis spectrophotometer using 1-cm quartz cells.

The distilled and deionized water was obtained from an AUTOSTILL 4000X system (JENCONS Scientific Limited) and then was twice distilled. pH measurements were carried out with a JENWAY 3010 pH meter.

Reagents

NA (purity: 99.5%) and NH_4VO_3 (purity: min. 99% proanalysis) were purchased from Merck and applied without further purification. In the voltammetric experiments, phosphate buffer (pH 7.4) was used as the supporting electrolyte. All solutions were prepared daily in triple-distilled and deionized water.

The phosphate buffer solution (pH 7.4) was obtained by adding appropriate amounts of 0.1 M NaOH to 0.1 M H_3PO_4 solution.

Procedures

Voltammetric procedure

The square-wave voltammograms were recorded using the following conditions (if not stated otherwise): scan rate was 200 mV s^{-1}, frequency was 100 Hz, and mercury drop size was medium (a surface area of 0.01765 cm^2), and an equilibrium time of 5 s was applied at the initial potential. The cyclic voltammograms were recorded using a scan rate of 500 mV s^{-1}, scan increment of 2 mV, an equilibrium time of 5 s, and a medium drop size, unless otherwise indicated.

Prior to each voltammetric experiment, a voltammogram of the solution containing only supporting electrolyte was measured. Solutions of NH_4VO_3 and NA in water were separately added to the cell containing

the supporting electrolyte and their voltammograms were recorded. The additions of NA to the cell containing NH_4VO_3 and vice versa were carried out, and the voltammograms were recorded. Solutions were deaerated for about 8 min with pure nitrogen gas before starting the electrochemical experiments. Each measurement was performed with a fresh mercury drop at room temperature.

Spectroscopic procedure

In the mole ratio method,[21] the solution containing the same amount of NH_4VO_3 was treated with increasing amounts of NA. The measured absorbance at 415 nm was plotted against the molar ratio of NA to NH_4VO_3. The NA to V ratio in the complex was found from the intersection of 2 extrapolated lines with different slopes.

Results and Discussion

Voltammetric studies

In the absence of NH_4VO_3, the voltammogram of the NA solution gives 2 reduction peaks (E_p = –1.48 V and –1.61 V) in the phosphate buffer (pH 7.4) (Figure 1). It was previously reported that NA reduced in 2 stages;[22] therefore, in a similar manner to the reduction of isonicotinic acid amide,[23] these peaks (–1.48 V and –1.61 V) can be attributed to the formation of aldehyde and carbinol derivatives of NA, respectively.[22]

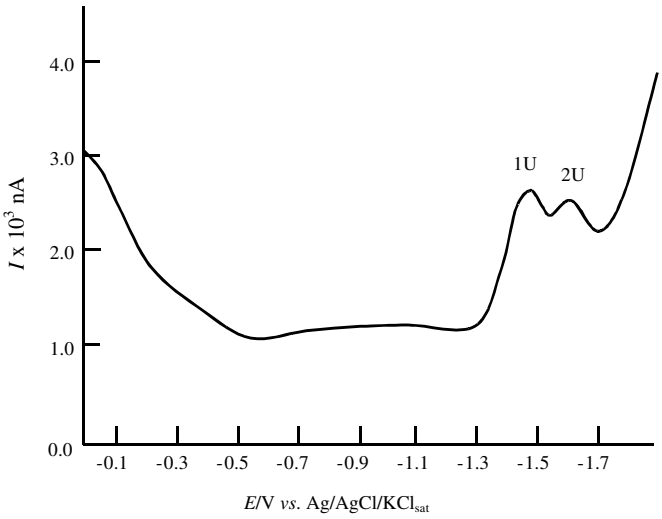


Figure 1. Square-wave voltammogram of 4.76×10^{-4} M NA solution in the phosphate buffer (pH 7.4). 1U: the formation of the aldehyde derivative of NA (–1.48 V); 2U: the formation of the carbinol derivative of NA (–1.61 V). Experimental conditions: scan rate: 200 mV s^{-1}; equilibrium time: 5 s; frequency: 100 Hz; drop size: medium.

In the phosphate buffer (pH 7.4), the cyclic voltammogram of NH_4VO_3 produced a quasi-reversible peak couple with E_{pc}/E_{pa} values at –0.14 V/–0.07 V (1U) and an irreversible reduction peak at –0.40 V (2U) (Figure 2). For NH_4VO_3, these peaks (–0.14 V and –0.40 V) are assigned to the reduction of V(V) to V(IV) and of V(IV) to V(III), respectively.[13]

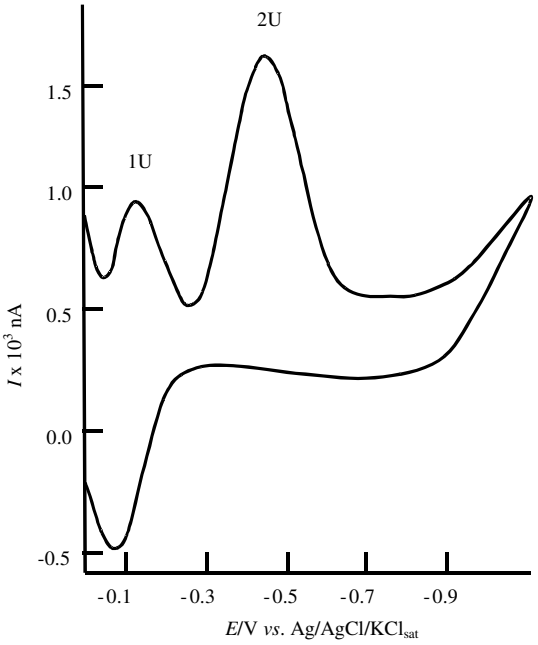


Figure 2. Cyclic voltammogram of 5×10^{-5} M NH_4VO_3 solution in the phosphate buffer (pH 7.4). 1U: the reduction of V(V) to V(IV); 2U: the reduction of V(IV) to V(III). Experimental conditions: scan rate: 500 mV s^{-1}; scan increment: 2 mV; equilibrium time: 5 s; drop size: medium.

The effect of NA on the voltammetric behavior of NH_4VO_3 is shown in Figure 3, in which curves 2 and 3 demonstrate the appearance of the new peak (at –0.35 V). Curves 2 and 3 in Figure 3 prove that the new peak does not occur in the absence of NA, even if NH_4VO_3 is present. The current of the new peak rises with the increase in NA concentration (Figure 3). Additionally, the current of a quasi-reversible peak at –0.14 V decreases with increasing NA concentration. At the same time, the second reduction peak (V(IV)/V(III)) of free NH_4VO_3 at –0.40 V shifts to a more negative potential (–0.50 V) in the presence of NA. The potential of this new peak is different from that of free V(V), so that the peak at –0.35 V may be due to the reduction of V(V) ions complexed with NA in the aqueous medium. The occurrence of the anodic counter part of the cathodic new peak at –0.35 V (Figure 3) clearly demonstrates that the electrode reaction of the vanadium complex has a reversible property. The peak-to-peak separation ($\Delta E_p = E_{pa} - E_{pc}$) for the new peak is about 60 mV, at a rate of 500 mV s^{-1} (Figure 3). This result suggests that the electrode process at –0.35 V has one-electron transfer.

Vanadium(V) characteristically gives 2 cathodic waves in acidic, neutral, and some complex-forming media, but only a single cathodic wave in strongly alkaline media.[24] In the former instance the first wave represents reduction to vanadium(IV), while the second wave has properties identical to those of the cathodic wave of vanadium(IV).[24] In some complexing media, such as neutral and weakly alkaline EDTA solutions, 3 cathodic waves are obtained, which correspond to stepwise reduction to vanadium(IV), vanadium(III), and vanadium(II). A single irreversible cathodic wave is obtained in alkaline media and usually represents reduction to vanadium(II).[24] Stepwise reduction of vanadium(IV) to vanadium(III) and vanadium(II) has been observed only in neutral and weakly alkaline EDTA, and in concentrated hydrochloric acid.[24] The V(IV)/V(III) system behaves irreversibly in the various media that have been investigated, and the reduction

of vanadium(IV) to vanadium(III) has been reported to be the rate-determining step in the overall reduction of vanadium(IV) to vanadium(II) in acidic media.[24] At potentials less negative than about –0.4 V the reduction proceeds only to vanadium(III), but at potentials more negative than about –0.6 V it proceeds practically completely to vanadium(II).[24]

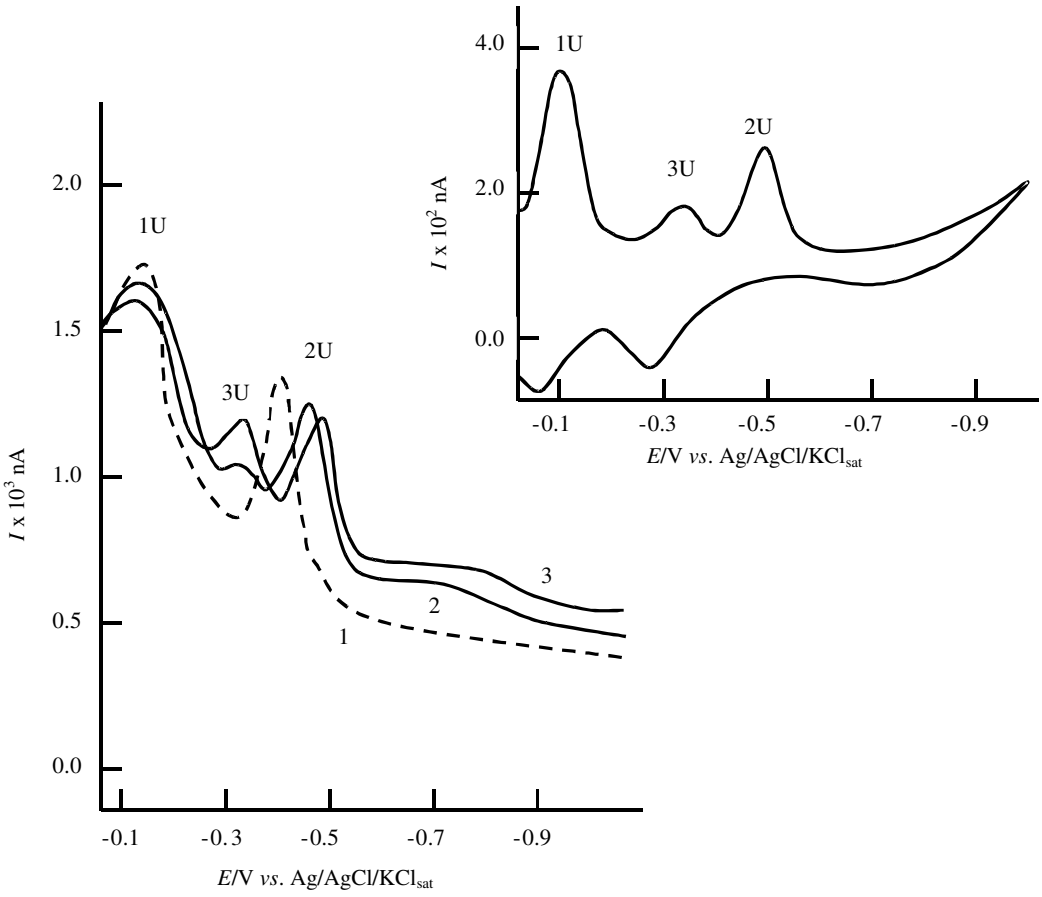


Figure 3. Square-wave voltammograms of 1×10^{-5} NH_4VO_3 solution in the absence (- - - - -) and presence (——) of 5×10^{-5}M (curve 2) and 1×10^{-4} M (curve 3) NA in 0.1 M phosphate buffer (pH 7.4). 1U: the first reduction peak of free NH_4VO_3; 2U: the second reduction peak of free NH_4VO_3; 3U: the reduction peak of V(V)-NA complex. Experimental conditions as in Figure 1 (Upper: cyclic voltammogram of 1×10^{-5} NH_4VO_3 solution in the presence 1×10^{-4} M NA. Experimental conditions as in Figure 2).

Therefore, the peak at –0.50 V probably corresponds to the irreversible reduction of the vanadium(IV) complex to vanadium(III). On the basis of voltammetric data, it can be said that the following reactions are taking place:

$$V(V) - NA + e^- \rightleftarrows V(IV) - NA(at - 0.35V)$$

$$V(IV) - NA + e^- \rightarrow V(III) - NA(at - 0.50V)$$

Spectroscopy

For final clarification of the complexation of NA with NH_4VO_3, electronic spectra measurements were performed. The UV-Vis spectra of NH_4VO_3, NA, and the mixture of NH_4VO_3 with NA were recorded in the 200-800-nm range in water. The maximum absorption bands are given in the Table. The electronic spectra of NA and NH_4VO_3 gave 3 (227, 238, and 261 nm) and 1 (266 nm) maximum absorption bands, respectively (Table). After the addition of NA to the NH_4VO_3 solution, some shifts in the band positions and new bands were observed (Figure 4 and Table).

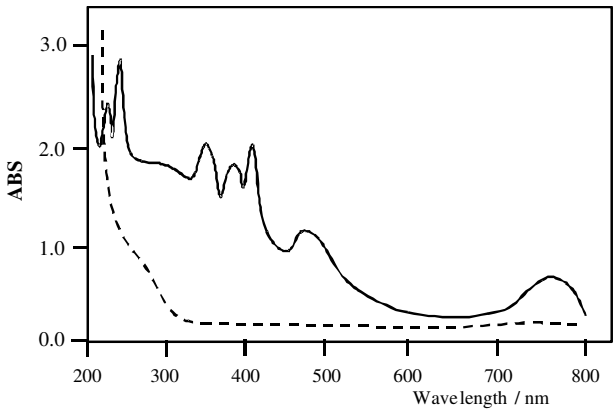


Figure 4. Absorbance spectra of 2×10^{-4}M NH_4VO_3 solution (- - - - -), and 1×10^{-4} M NH_4VO_3 in the presence of 2×10^{-4} M NA solution (——-).

Table. Characteristic absorption maxima (nm) data of NH_4VO_3, NA, and mixture of NH_4VO_3 with NA in aqueous solution.

NH_4VO_3 (1×10^{-3}M)	NA (1×10^{-3}M)	NH_4VO_3 + NA mixture
266 (sh)	261	771
	238	480
	227	415
		398
		373
		259
		247

sh: shoulder

The VO_3^- ion has d^0 configuration (V^{+5}) and therefore no d-d transitions are observed. On the other hand, it is consistent with the 2 ligand-to-metal charge transfer (LMCT) transition ranges of 475-550 nm[25,26] and 550-800 nm[27] reported in some d^0 oxovanadium complexes, and these can be assigned to LMCT transitions from phenolate oxygens to empty d orbitals on vanadium.

Pal et al.[28] reported that the pervanadyl (VO_2^+) complexes with N-(aroyl)-N′-(picolinylidene) hydrazines displayed 3 strong absorptions in the ranges of 486-405, 341-285, and 290-233 nm due to LMCT and intraligand transitions. Moreover, the band located at 650 nm in the spectra of the oxovanadium(V) complexes ([$VO(ferron)_2OH$], [$VO(ferron)_2OCH_3$]) was attributed to a charge transfer from a delocalized

ring π-orbital to the metal center.[29] In the electronic spectrum of the $[(VOL2)_2(OCH_3)_2]$ (where H_3L2: bis-3,5-(2′-hydroxyphenyl)-1H-1,2,4-triazole) complex in the presence of HPF_6, only minor changes in the absorptions assigned to intraligand transitions ($\pi \rightarrow \pi*$) were observed ($<$ 450 nm), whereas a red shift from 554 to 705 nm was observed.[30] The low-energy absorption between 600 and 750 nm was assigned as an LMCT transition.[30] In addition, Paine[31] reported that $V^VO(L^{PO})(HL^{PO})$ and $V^VOL^{Se}(\mu\text{-OH})]_2$ complexes (where H_2L^{Se}: 2, 2′-Selenobis(4, 6-di-*tert*-butylphenol), and H_2L^{PO}: 2, 2′-Phenylphosphineoxidebis(4, 6-di-*tert*-butylphenol)) gave λ_{max} values at 395, 537, and 721 nm, and at 511 and 788 nm, respectively. In the analyzed region, intra-ligand transitions at higher energies and charge transfer (CT) transitions at intermediate energies were expected to be found.[31] The purple color of these complexes was presumably due to a phenolate-to-vanadium charge transfer.[31]

Therefore, the bands at 771 and 480 nm (Table) can be attributed to LMCT transitions. Moreover, the higher energy transitions at 415, 398, and 373 nm, which are absent in the free NA, are also assigned to LMCT transitions involving the organic ligand by analogy with other reported vanadium(V) complexes. The band at 373 nm essentially involves the oxygen atom, whereas the other one at 398 nm may be due to the nitrogen atom.[32]

On the other hand, in the electronic spectra of the mixture of NH_4VO_3 with NA, it was shown that the band at 261 nm of NA shifts to 259 nm. Upon raising the NH_4VO_3 concentration, a distinct increase in the intensity of the 259 nm band supports the assumption of binding to the NA. The absorption band at higher energies (247 nm) can be assigned to intraligand transitions, probably superimposed with the O→V charge transfer involving the double bonded oxo group.[32,33]

Agnihotri et al.[34] measured the absorbance values at 420 nm to determine the metal-to-ligand ratio of the vanadium(V)-CHMTC complex (where CHMTC is 6-chloro-3-hydroxy-7-methyl-2-(2-thienyl)-4H-chromen-4-one). In the present study, the metal:ligand ratio of V(V)-NA complex in the aqueous medium was determined to be 1:2 by measuring the absorbance at 415 nm, according to the mole ratio method (Figure 5).

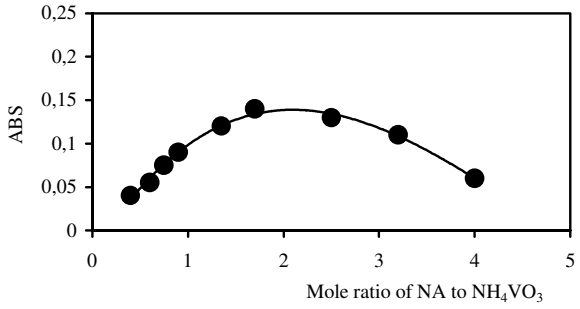


Figure 5. Plot of the absorbance at 415 nm versus the mole ratio of NA to NH_4VO_3.

Conclusion

Voltammetric studies of the interaction of vanadium(V) with NA showed that there is a complex formation between vanadium(V) and NA at physiological pH, which is then followed by the reduction of vanadium(V) to vanadium(IV) and vanadium(IV) to vanadium(III). Electronic spectroscopy measurements proved that the complex of V(V) with NA is of ML_2 type. This study on the binding of vanadium to NA will contribute

to a better understanding of the behavior of vanadium in biological systems.

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