Turk J Chem
33 (2009) , 507 – 520.

doi:10.3906/kim-0812-16

Study of binary complexes of nickel(II), copper(II), and vanadium(V) with acetazolamide in aqueous medium by voltammetry

İclal BULUT
Department of Chemistry, Faculty of Arts and Sciences, Ondokuzmayıs University, Kurupelit, 55139, Samsun-TURKEY
e-mail: iclalb@omu.edu.tr

Received 04.12.2008

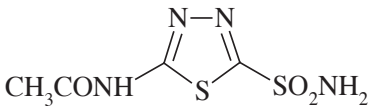
The voltammetric behaviour of acetazolamide, the systemic carbonic anhydrase inhibitor, in the presence of some metal ions (Cu(II), Ni(II), and V(V)) were investigated using square-wave and cyclic voltammetry in physiological pH (pH 7.4). Square-wave voltammogram of acetazolamide in the absence of metal ions gave only 1 reduction peak at -1.65 V attributed to a catalytic hydrogen peak. Three reversible peaks at -0.068, -0.262, and -0.434 V were observed for the solutions containing both copper(II) ions and acetazolamide in the SWV. The peak at -0.434 V was attributed to Cu(II)-acetazolamide complex. In the presence of acetazolamide, copper-acetazolamide complex formation was proved by a reversible peak with 2 electron transfers at -0.450 V. Complex formation of an adduct of trioxovanadate(V) with acetazolamide onto dropping mercury electrode was followed by a reduction peak at -0.480 V. Ni(II)-acetazolamide complex was observed to reduce at the more positive potential (-0.830 V) than that of the hydrated Ni(II) ions (-1.200 V) implying that acetazolamide is a catalyst for Ni(II) reduction at a mercury electrode. The UV-vis spectra of all the acetazolamide complexes were also discussed.

Key Words: Acetazolamide; Copper; Nickel; Vanadium; Binary complexes; Electronic Spectra; Voltammetry.

Introduction

Aromatic sulfonamides and their derivative compounds with 1,3,4-thiadiazole constitute an important group of carbonic anhydrase inhibitors. The inhibition of this enzyme by sulfonamide drugs finds clinical application in the treatment of glaucoma, epilepsy, and other disorders. On the other hand, these compounds have also played an important role in the physico-chemical and enzymatic studies on carbonic anhydrase.[1]

The systemic carbonic anhydrase inhibitor (CAI), acetazolamide {5-acetamido-1,3,4-thiadiazole-2-sulfonamide} (ACZ) (Scheme 1), is generally used for the treatment of glaucoma [2,3] and epilepsy[4,5] and also as diuretic.[6]



Scheme 1. Chemical structure of acetazolamide.

Metal ions play an important role in altering biochemical properties of the sulfonamide based drugs, and indicate a new direction in the impact of chemotherapeutic agents and lowering toxicity. The studies have proved that the metal complexes of sulfonamides possess much stronger CAI properties than the sulfonamides themselves from which they were prepared.[7–9] Some metal complexes of 1,3,4-thiadiazole derivatives have been reported as in vitro inhibitors of the zinc enzyme carbonic anhydrase,[10] whereas in vivo studies showed good antiepileptic action for some Cu(II) and Zn(II) complexes of the sulfonamide type ligands.[11] Finally, some 2,5-disubstituted -1,3,4-thiadiazoles as well as their Cu(II) complexes were reported to act as fungitoxic agents.[12] These properties obviously originate from the binding mode of metal ions that may cause a significant influence on the redox properties of these drugs. Therefore, the studies on acetazolamide as a sulfonamide derivative and its metal complexes have been reported in the literature.[13,14]

The apparent formula of acetazolamide is given in Scheme 1. As can be seen from Scheme 1 that its metal-complexation can be formed by means of acetamide and/or sulfonamide NH groups as monoanion and dianion for the metal ions which can be crucially important in biological processes.[15,16] Although the spectroscopic and thermal characterization studies of metal(II)-acetazolamide complex have been carried out to illuminate the interaction processes,[17,18] no voltammetric studies about the acetazolamide-metal interaction were reported in the literature. Voltammetry ensures important information on the interactions of the ligands with the metal ions.[19,20] Many of the most important biological processes are based on redox processes and there are similarities between electrochemical and biological reactions concerning electron transfer. Therefore, electrochemical studies may provide evidence regarding the mechanisms of biological processes.

In this context this study completes the lack of information about the voltammetric behaviours of acetazolamide in the presence and absence of Cu(II), Ni(II), and V(V) ions. The other reason for using this compound is that its resemblance to a range of biologically-active molecules (enzymes, proteins) that contain tiolic groups, molecules that are implicated in cellar or tissular redox-reactions. In this case, acetazolamide can be used as models to establish some relations between the electrochemical properties and the pharmacological ones, or the biological action or behaviour of some drugs or chemical species with biochemical significance. The investigation of the complexes of metal ions (such as copper, nickel, and (oxo)vanadium), which are vital for biological systems, is also important because these complexes may serve in clarification of clinical results and as models for studying the role of metal ions in biological systems.

Experimental

Reagent

Stock solution of acetazolamide, (1×10^{-3} M) was prepared by dissolving the appropriate amount of the compound in a small amount of methanol, and diluted to 100 mL with deionized distilled water. $CuCl_2$, $NiCl_2$, and NH_4VO_3 solutions were also prepared in deionized distilled water. Britton-Robinson buffer (pH 7.4) was used as the supporting electrolyte. Britton-Robinson buffer was prepared by adding sodium hydroxide solution (0.5 mol L^{-1}) in to 100 mL of mixed acid, containing 0.04 mol L^{-1} of each of boric acid, ortho-phosphoric acid and acetic acid. All chemicals were analytical grade reagents and all the solutions were prepared with deionized triply distilled water.

Apparatus

The square wave and cyclic voltammetry experiments were carried out with an EG&G PAR model 384 B polarographic analyser equipped with a PARC 303A cell stand (EG&G). A 3-electrode cell, containing a static mercury electrode (SMDE) as working electrode, an Ag|AgCl| sat. KCl electrode as reference electrode, and a platinum wire as auxiliary electrode was employed for the electrochemical measurements.

A digital pH meter (Crison 2000 micropH) was used for preparing buffer solutions, which were the supporting electrolyte in voltammetric experiments. A pH meter equipped with an Ag|AgCl| glass combination pH electrode was used.

Procedure

Before each measurement the solutions were de-aerated by a stream of pure nitrogen. During the measurements, nitrogen was passed above the solutions in the cell. A known volume of a standard solution of acetazolamide was added to the voltammetric cell, which was closed, deaerated, and blanketed with oxygen-free nitrogen. The addition of metal ions to the cell containing the acetazolamide and vice-versa were carried out and the voltammograms were recorded. All experiments were carried out at ambient temperature (approx. 20 °C). The potential scans were recorded using the square-wave and cyclic voltammetry modulations and the following optimum parameters (if not stated otherwise): pulse height, 20 mV; frequency, 100 Hz; drop size, medium and equilibrium time 5 s. Each measurement was carried out on a fresh mercury drop.

Result and discussion

The voltammetric behaviour of acetazolamide

Acetazolamide has 2 ionisable groups: carbonamido and sulfonamido groups. Although the proximity between the pKa_1 (7.52) and pKa_2 (9.41) values of these groups suggests that both deprotonations occur simultaneously and establish equilibrium, it was reported that the first deprotonation of acetazolamide takes place on the carbonamido moiety[1] and only one ionization equilibrium occurs in the pH range from acidic medium to pH

8.7-8.8 for acetazolamide.[21] It is the reason that the electrochemical studies were carried out at pH 7.4. The selected pH value is also close to the isoelectric point (7.2).

The voltammetric behaviour of acetazolamide in the absence of metal ions (Cu(II), Ni(II), and V(V)) is shown in Figure 1. It can be clearly seen in Figure 1 that acetazolamide gives 1 reduction peak at -1.65 V inferred from the catalytic formation of hydrogen. From the voltammetric data, the electrode mechanism involves cleavage of C-S bond and may be suggested as follow:[22]

$$ArSO_2NH_2 + 2e^- + 1H^+ \rightarrow ArH + SO_2NH_2^-$$

$$SO_2NH_2^- + H_20 \rightarrow H^+ + SO_3^{2-} + NH_3$$

$$H^+ + e^- \rightarrow {}^1/_2\ H_2$$

It is observed that the peak potential at -1.65 V shifts slightly towards more negative potentials by increasing the concentration. The cyclic voltammogram of this reduction peak at pH 7.4 (Figure 1) was not accompanied by an anodic peak indicating that the redox reaction is totally irreversible.

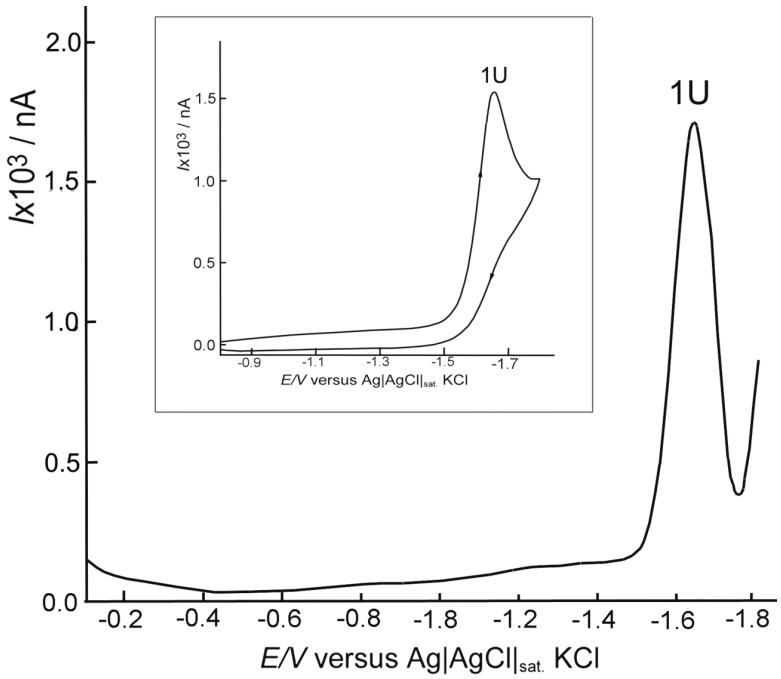


Figure 1. Square-wave voltammogram of 1.5×10^{-4} M acetazolamide at 0.04 M Britton-Robinson buffer (pH 7.4). Inset: Cyclic voltammogram of 1.5×10^{-4} M acetazolamide. Experimental conditions: pulse height, 20 mV; frequency, 100 Hz; drop size, medium, scan rate, 200 mV s^{-1} and equilibrium time, 5 s.

The effects of the potential scan rate, ν, on the peak current, i_p, and peak potential, E_p, were studied. Cyclic voltammetry at different scan rates, ν (50-1000mV s^{-1}), showed that the peak currents of acetazolamide were proportional to square root of scan rate $\nu^{1/2}$ at static mercury electrode, as predicted for a diffusion-controlled regime (for 2×10^{-4} M acetazolamide i_p (nA)= $104.93\nu^{1/2}$ (mV s^{-1}) + 1201.58 (r^2 = 0.9995)).

E_p shifting to more positive potentials was also observed when the scan rate increased which confirms the irreversibility of the reduction process.

At pH 7.4, the straight line calibration curve of acetazolamide corresponded to the equation: i_p = -13.26 + 1.04x10^7 [Acetazolamide] (r^2 = 0.9988) for concentrations of 5.0 × 10^{-6} - 2.5 × 10^{-4}, where i_p is expressed in nA and the concentration is in M. Thus, the peak at -1.65 V can be used for analytical purposes.

The effect of pH on the voltamperometric study was investigated by recording SW voltammograms of acetazolamide (1 × 10^{-5} M) at pH values ranging from 2 to 12 and 2 irreversible peaks at pH values lower than 3 were observed. The first peak at more positive potential (-0.59 V) is attributed to the reduction of the azomethine group (C=N-) in the acetazolamide, whereas the second peak (-1.07 V) is due to the catalytic hydrogen wave. These 2 peaks were also observed by Balugera et al. in a related study of acetazolamide.[23] Nevertheless they could use of first peak (-0.59 V) and were not able to measure the second peak at pH 1.65. The peak potentials and peak currents of acetazolamide were also investigated and found to be pH-dependent. It is noticed that the first peak of acetazolamide above pH 3 disappears as proved by the study of Balugera et al.[23] As pH increased, the second peak shifted towards more negative potentials (Figure 2A), whereas the peak current decreased (Figure 2B). In excess alkali medium (pH ≥ 11), the peak current was observed to decrease to zero.

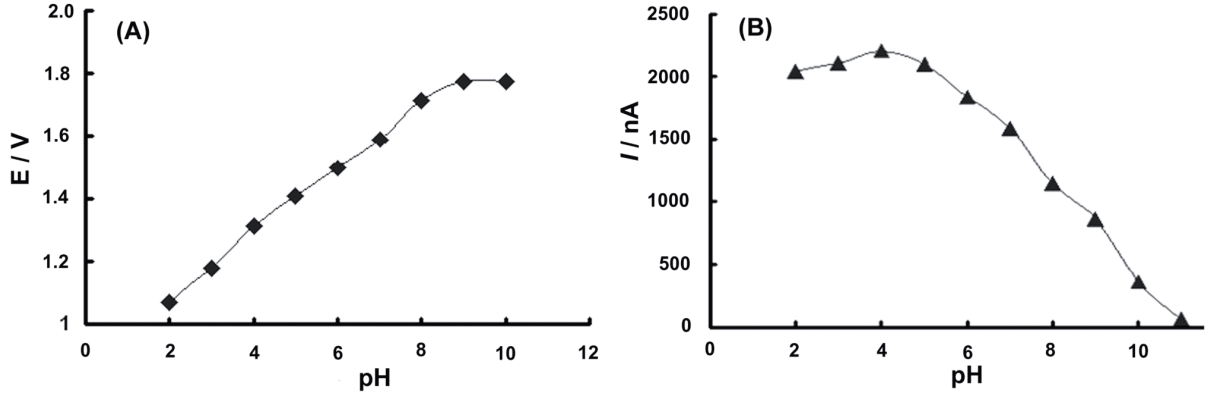


Figure 2. The dependence of square-wave peak potential (A) and peak current (B) of 1.5 × 10^{-4} M ACZ on pH. Other conditions are as in Figure 1.

Acetazolamide in the presence of Cu(II) ions

At physiological pH (7.40), square-wave voltammograms of 1 × 10^{-5} M Cu(II) solution gave a reversible peak at -0.172 V. This peak can be inferred from the reduction of free Cu(II) ions to the amalgam (Cu(II) +2e$^-$ ⇔ Cu(Hg)). When acetazolamide was added to the 1 × 10^{-5} M Cu(II) solution, over the potential range of 0.000 to -0.800 V, 3 reversible peaks at -0.068, -0.262, and -0.434 V were observed (Figure 3).

The peak at -0.068 V was out of the working range with subsequent additions of acetazolamide. The peaks at -0.068 and -0.262 V are inferred from the 2-stage reduction of Cu(II) ions in the presence of the ligand. The peak at -0.434 V can be attributed to the reduction of Cu(II)L_2 complex to the copper metal. With increasing acetazolamide concentration, the potential of this peak at -0.434 V is shifted towards slightly

negative potentials and fixed at -0.450 V with a well-defined shape (Figure 4). The peak current of the cathodic peak at -0.450 V showed a linear increase up to the acetazolamide concentration of 1.1 × 10^{-4} M; however, above this concentration, a plateau region was observed. As can be seen from cyclic voltammogram in Figure 3, the anodic peak of Cu(II)-acetozolamide complex was clearly observed, but $I_{pc} > I_{pa}$ is due to the weak adsorption of the Cu(II)-acetazolamide complex. The reduction of the complex was a result of a reversible process due to the difference of potentials $\Delta E_{p(a-c)} \approx 36$ mV in which 2 electrons are transferred.[24]

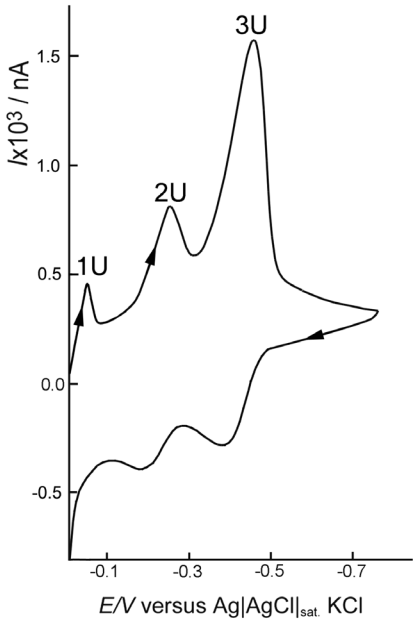


Figure 3. Cyclic voltammogram of 1 × 10^{-5} M Cu(II) containing 2.5 × 10^{-4} M acetazolamide. 1U, the reduction of Cu(II)L to Cu(I)L (-0.068 V); 2U, the reduction of Cu(I)L to Cu(Hg) (-0.262 V); 3U, the reduction of $Cu(II)L_2$ complex to Cu(Hg) (L= ACZ) (-0.45 V). Other conditions are as in Figure 1.

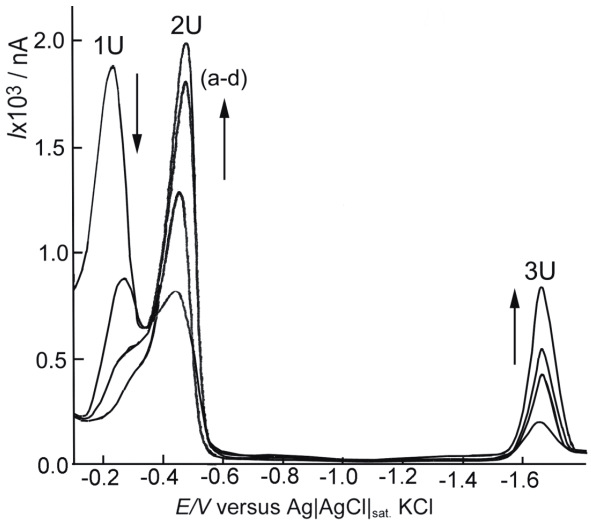
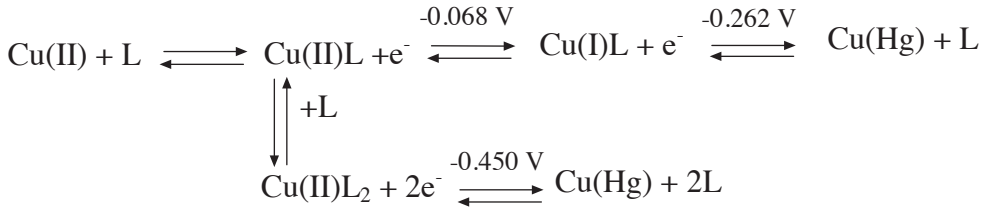


Figure 4. Square-wave voltammograms of 1 × 10^{-5} M Cu(II) solution containing 5 × 10^{-5} M (a); 7 × 10^{-5} M (b); 10 × 10^{-5} M (c); 15 × 10^{-5} M (d) acetazolamide at 0.04 M Britton-Robinson buffer (pH 7.4). 1U, the reduction of Cu(II) (-0.172 V); 2U, the reduction of Cu(II)-acetazolamide complex (-0.45 V); 3U, the reduction of acetazolamide (-1.65 V). Other conditions are as in Figure 1.

As can be seen in Figure 3, acetazolamide forms the complexes of both Cu(I) and Cu(II) ions. The observation of 2-stage reduction (Cu(II)⇔Cu(I) and Cu(I)⇔Cu(0)) of copper ions depends on the structure of the ligand.[25] If preferential stabilisation of copper(I) species takes place due to complex formation, a redox reaction in 2 steps will occur, i.e., Cu(II) + $1e^-$ ↔ Cu(I) and Cu(I) + $1e^-$ ↔ Cu(0) instead of the direct reaction Cu(II) + $2e^-$ ↔ Cu(0).[26] However, stabilization of Cu(I) species may also be due to d-π interactions between the copper-d orbitals and the aromatic π-system rather than binding of the metal with the carbonamide or/and sulphonamide.[15,16]

From the voltammetric data the electrode mechanisms of these peaks can be suggested as follows:



Scheme 2. Reduction pathway in the copper(II)-acetazolamide complex,where L is acetazolamide.

The binding of acetazolamide to Cu(II) occurs mainly via sulfonamido N atom and N atom of the thiadiazole ring in both aqueous solution[27] and solid state.[28]

Acetazolamide in the presence of V(V)

The square-wave voltammogram of 4×10^{-5} M NH_4VO_3 in the absence of ligand gave 3 cathodic peaks at -0.228, -0.636, and -1.443 V in the potential range from -0.100 to -1.800 V at pH 7.4 (Figure 5).

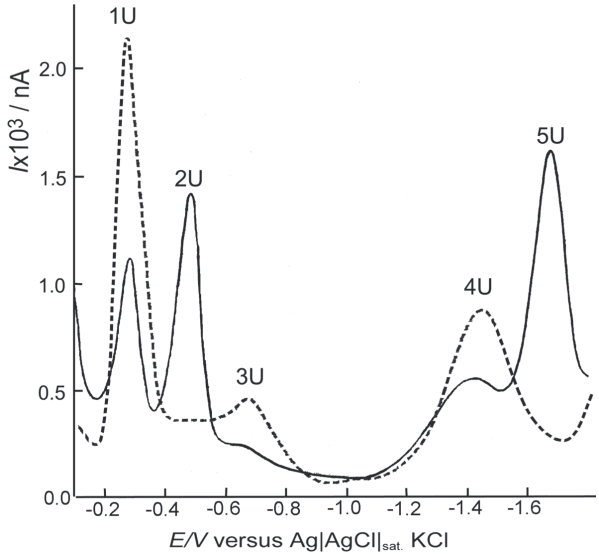


Figure 5. Square-wave voltammograms 4×10^{-5} M NH_4VO_3 solution in the absence (- - - -) and presence (——) of 2.5×10^{-4} M acetazolamide at 0.04 M Britton-Robinson buffer (pH 7.4). 1U, the reduction to V(IV) of V(V) (-0.228 V); 2U, the reduction of V(V)-acetazolamide complex (-0.48 V); 3U, the reduction to V(III) of V(IV) (-0.636 V); 4U, the reduction to V(II) of V(III) (-1.443 V); 5U, the reduction of acetazolamide (-1.65 V). Other conditions as in Figure 1.

As can be seen in Figure 6, the cathodic peak at -0.228 V has an anodic counterpart, whereas the other cathodic peaks (-0.636 and -1.443 V) did not give any peak in the anodic branch. The potential difference of the cathodic and anodic peaks of the peak couple at -0.228 V shows that this electrode process is irreversible similar to the others. For the peak couple at -0.228 V, the difference between the currents of cathodic and anodic peaks shows that this electrode process is affected by adsorption. The peaks at -0.228 and -0.636 V are attributed to reduction of vanadium(V) to vanadium(IV) and vanadium(III), respectively. The peak at -1.443 V is assigned to the reduction of vanadium(IV) of vanadium(II).

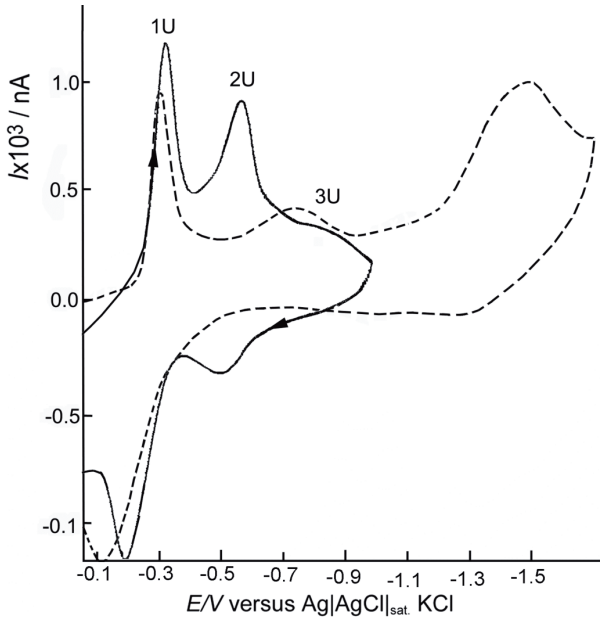


Figure 6. Cyclic voltammogram of 4×10^{-5} M NH_4VO_3 solution in the absence (- - - -) and presence (——) of 1.5×10^{-4} M acetazolamide. 1U, the reduction to V(IV) of V(V) (-0.228 V); 2U, the reduction of V(V)-acetazolamide complex (-0.48 V); 3U, the reduction to V(III) of V(IV) (-0.636 V). Other conditions are as in Figure 1.

The peak at -1.443 V is assigned to the reduction to vanadium(II) of vanadium(IV). It was reported that vanadium (V) characteristically gives 2 cathodic waves in acidic, neutral, and some complex-forming media, but only a single cathodic wave in strongly alkali medium.[29] The first wave represents reduction to vanadium(IV), while the second wave has properties identical to those of the cathodic wave of vanadium (IV).[29] In some complexing media, such as neutral and weakly alkaline EDTA solutions, 3 cathodic waves are obtained, which corresponds 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).[29] 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.[29] At potentials more negative than about -0.6 V it proceeds completely to vanadium(II).[29]

The effect of acetazolamide on the voltammetric behaviour of NH_4VO_3 is shown in Figure 5. Addition of acetazolamide into the cell containing 4×10^{-5} M V(V) solution led to a decrease in the current of the peaks of free V(V) and the formation of a shoulder at -0.432 V (Figure 5). With increasing acetazolamide concentration, the potential of the peak at -0.432 V is shifted towards more negative potentials and fixed at -0.480 V. As a result of the increasing predominance of vanadium complex, the peak current of this new peak increased with subsequent additions of acetazolamide. The peak at -0.480 V probably originates from the reduction of V(V)-acetazolamide complex in the aqueous medium.

The reversibility of the electrochemical reaction of V(V)-acetazolamide complex has been studied by cyclic voltammetry in the potential range from -0.100 to -1.200 V (Figure 6). The occurrence of the anodic

counter part of the cathodic new peak at -0.48 V (Figure 6) clearly demonstrates that the vanadium complex shows a reversible reduction process. The separation between the anodic and cathodic peaks in the cyclic voltammograms of the complex is *ca.* 30 mV which is very close to the theoretical value (28 mV) and corresponds to the 2-electron reduction.[24] On the basis of voltammetric data, the following reaction mechanism is taking place:

$$\text{V(V)-acetazolamide} + 2e^- \rightleftharpoons \text{V(III)-acetazolamide (at -0.48V)}$$

Acetazolamide in the presence of Ni(II) ions

The square-wave voltammogram of 1×10^{-4} M $NiCl_2$ solution in the absence of acetazolamide produces a cathodic peak at -1.20 V at pH 7.4. The peak at -1.20 V was inferred from irreversible reduction of the hydrated Ni(II) ions. The catalytic nickel reduction in the presence of acetazolamide gives a maximum current at a pH 7.4. At pH values above 7.4, the peak current decreases, probably owing to the hydrolysis of nickel ion. This assumption is supported in the absence of acetazolamide, which shows a strong effect of high pH on both the shape and height of the cathodic nickel peak. It was noticed from the experimental steps that the peak current of the hydrated Ni(II) ions decreases with addition of the acetazolamide to the cell containing 5×10^{-5} M Ni(II) ions and that of the acetazolamide simultaneously increases. In addition, a new cathodic peak (-0.85 V) at more positive potential than that of hydrated Ni(II) ions appeared. With increasing acetazolamide concentration ($1 \times 10^{-5} - 3 \times 10^{-4}$ M), the potential of this new peak is shifted towards more positive potential and fixed at -0.83 V (Figure 7, 1U). The peak at -0.83 V is explained as catalytic prewave. This means that acetazolamide catalyses the reduction of the complexed Ni(II) ions at -0.83 V.

For the peak at -0.83 V, the plot of Ip / $\nu^{1/2}$ versus ν was constructed (Figure 8). As can be seen in Figure 8, the Ip / $\nu^{1/2}$ value decreases by increasing scan rate (v). This result supports that the peak at -0.83 V has a catalytic property [30].

Normally, with the addition of increasing concentration of a ligand, the reduction peak potential of metal ion generally shifts to more negative potentials and also the reduction of the metal complex ion becomes more difficult due to stabilization of metal ion by complex formation. However, the reduction of hydrated Ni(II) ions has a large overpotential, in the presence of certain ligands present at the trace levels, the overvoltage is decreased and the reduction occurs at more positive potential than that of the aquaion. This case is generally observed in the chelate complexes of Ni(II) ions with nitrogen containing ligands like NH_3, pyridine, or nicotinamide.[31,32] Acetazolamide has 3 coordination sites, namely acetamide N, sulfonamide N, and thiadiazole N atom. The peak observed at more positive potential (-0.83 V) than that of the hydrated Ni(II) ions (-1.20 V) is evidence that the binding of acetazolamide to Ni (II) occurs mainly via N atoms in the compound rather than sulfonyl-O or carbonyl O atoms.[33]

This complex formation was also supported by the cyclic voltammetry experiments (Figure 9). The irreversibility of the peak at -0.83 V was determined from the cylic voltammogram (Figure 9, 1U). E_p shifting to more positive potentials was observed when the scan rate increased which confirms the irreversibility of the reduction process.

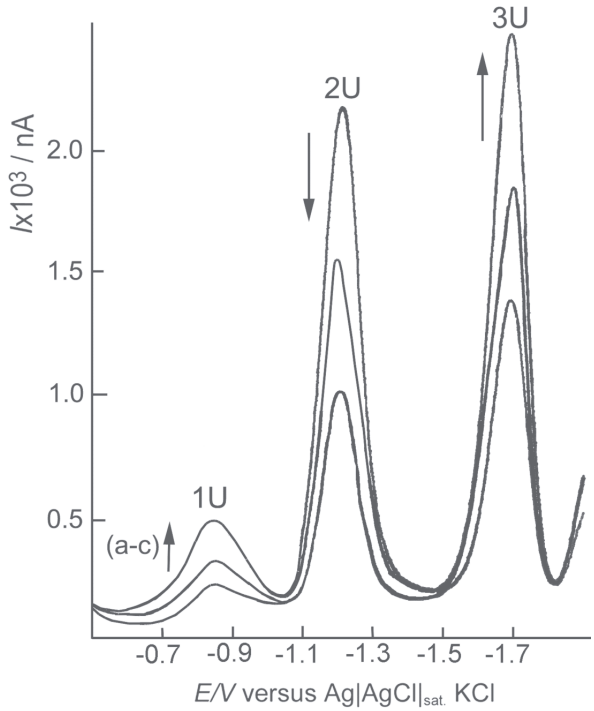


Figure 7. Square-wave voltammograms 1×10^{-4} M Ni(II) solution containing 1.5×10^{-4} M (a); 2.25×10^{-4} M (b); 3×10^{-4} M (c) acetazolamide at 0.04 M Britton-Robinson buffer (pH 7). 1U, Catalytic pre-wave due to the reduction of Ni(II)-acetazolamide complex (-0.83 V); 2U, the reduction of Ni(II) ions (-1.20); 3U , the reduction of acetazolamide (-1.65 V). Other conditions as in Figure 1.

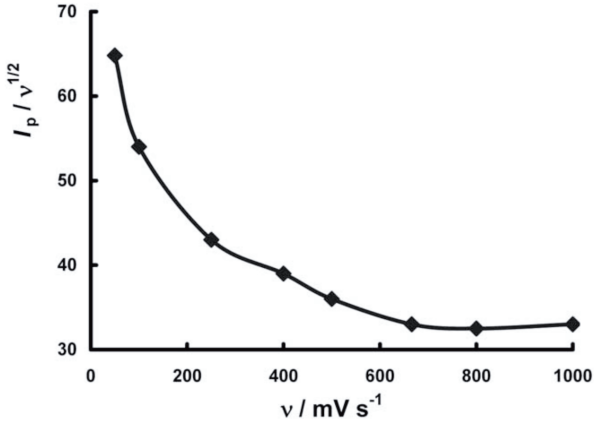


Figure 8. Plot of Ip / $\nu^{1/2}$ v.s. ν of catalytic nickel peak.

As a result, the irreversible peak, which is more positive potential (-0.83 V) than that of the hydrated Ni(II) ions (-1.20 V), originates from the catalytic reduction of complexed Ni(II) with acetazolamide.

Electronic Spectra

In order to clarify the nature of transformations of this redox reactions and metal complexes, the electronic spectra of the metal-acetazolamide solutions were also investigated and the results obtained were given in Figure 10. The electronic spectra of acetazolamide in water consist of 3 absorption maxima at 264, 280, and 302 nm and are in agreement with the literature data.[1] After addition of metal ion (V(V), Cu(II), and Ni(II)), the spectrum of acetazolamide solution was also recorded, some shifts in the band positions were observed (Figure 10). The shifts observed in the UV-Vis spectra can be attributed to coordination effects.

The electronic data of the dark green Cu(II)-acetazolamide solution gave 5 absorption bands at 322, 344, 363, 385, and 661 nm apart from the acetazolamide bands (255, 285, and 303 nm). The higher energy peaks (322, 344, 363, and 385 nm) can be assigned to ligand-to-metal charge transition (Figure 10 (a)).The lower energy band at 661 nm can be attributed to a d-d transition in Cu(II) associated with the formation of Cu-N bonds.[34] The position and the intensity of the d-d band is characteristic for Cu(II) complexes with a octahedral

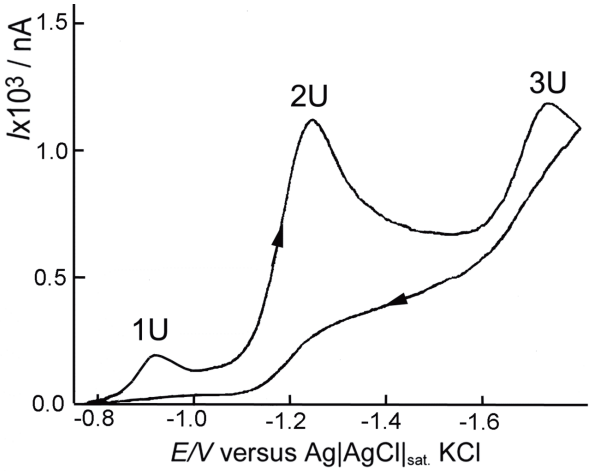


Figure 9. Cyclic voltammogram of 1×10^{-4} M Ni(II) containing 3×10^{-4} M acetazolamide. 1U, Catalytic prewave due to the reduction of Ni(II)-acetazolamide complex (-0.83 V); 2U, the reduction of Ni(II) ions (-1.20); 3U , the reduction of acetazolamide (-1.65 V).

symmetry.[34] The complex formation of copper(II) with acetazolamide was observed in both solution[27] and solid state.[28] The electronic spectra obtained in this study also supports the complex formation of Cu(II)-ACZ from the shift at d-d transition.

A solution of V(V)-acetazolamide in water gave 4 absorption bands at 236, 254, 279, and 306 nm, which are assigned to the ligand to ligand charge transition (LLCT) (Figure 10 (b)). Upon addition the NH_4VO_3 solution, a distinct increase in the intensity of the band supports the assumption of binding to the acetazolamide. The other absorption bands (319, 332, 360, and 424 nm), which are absent in the free acetazolamide, are related to ligand-to-metal charge transition (LMCT) involving the organic ligand by analogy with other reported vanadium (V) complexes.[35] The band at 319, 332, and 360 nm essentially involves the oxygen atom, whereas the other one at 424 nm may be due to the nitrogen atom.[35] Vanadium (V) has a $3d^{\circ}$ configuration, and therefore no d-d bands are expected. Pat et al. reported that the pervanadyl (VO_2^+) complexes with N-(aroyl)-N-(picoliylidene) hydrazines displayed 3 strong absorptions in the ranges of 485-405, 341-285, and 290-233 nm due to LMCT and intraligand transitions.[36] Acetazolamide is known to have a varied coordination chemistry with metal ions as a monoanion[15] or dianion[16]. For monoanion either acetamide or sulfonamide NH group is deprotonated. For the dianion, both acidic NH groups are deprotonated. The LMCT transition is considered as a charge transfer from sulfonamide N,O and/or carbonamide N,O atoms of acetazolamide to empty d orbitals on the vanadium.

The Ni(II)-acetazolamide complex in water showed 3 electron bands at 313, 376, and 640 nm different from the acetazolamide bands (259, 279, and 298 nm) (Figure 10 (c)). The higher energy bands at 313 and 376 nm could be assigned to ligand-to-metal charge transition. The LMCT band at 376 nm can be attributed to N→Ni charge transfer, while the other band at 313 nm is also due to LMCT arising out of O→Ni charge transfer.[37] The broad band at 640 nm is ascribed to the d-d transition and is characteristic for the 6-coordinated Ni(II) complex.

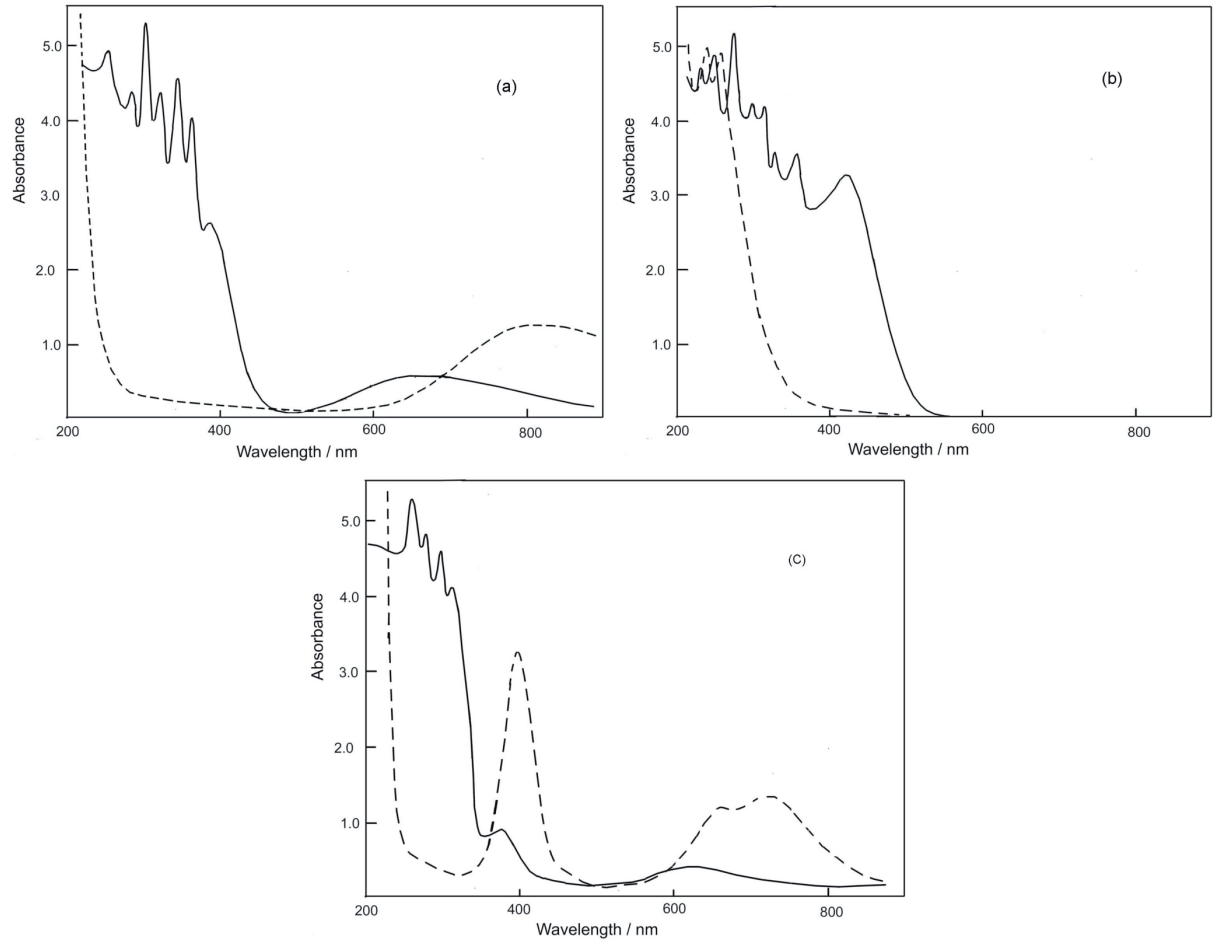


Figure 10. Electronic spectra of metal-acetazolamide system (a) Electronic specta of 1×10^{-2} M Cu(II) solution (- - -). Electronic spectra of 4×10^{-3} M Cu(II) in the presence of 1×10^{-2} M Acetazolamide (——). (b) Electronic spectra of 2×10^{-3} M NH_4VO_3 solution (- - -). Electronic spectra of 6×10^{-3} M NH_4VO_3 in the presence of 1×10^{-2} M Acetazolamide (——). (c) Electronic spectra of 1×10^{-2} M Ni(II) solution (- - -). Electronic spectra of 5×10^{-3} M Ni(II) in the presence of 1×10^{-2} M Acetazolamide (——).

These results clearly indicate that the acetazolamide coordinate to metal ions, which is in accordance with the results of the voltammetric study.

Acknowledgement

The author gratefully acknowledges the support of this work by TÜBİTAK-BİDEB. She is also grateful to Dr. Ahmet Bulut and Dr. Ender Biçer (Ondokuz Mayıs University, Samsun) for their valuable contributions.

References

1. Chufán, E.E.; Suvire, F.D.; Enriz, R.D.; Pedregosa, J.C. *Talanta*, **1999**, *49*, 859-868.
2. Kaur, I.P.; Smitha, R.; Aggarwal, D.; Kapil, M. *Int. J. Pharm.* **2002**, *248*, 1-14.
3. Sabri, K.; Levin, A. V. *JAAPOS.* **2006,** *10,* 464-468.
4. Lim, L.L.; Foldvary, N.; Mascha, E.; Lee, J. *Epilepsia,* **2001,** *42*, 746-749.
5. Varadkar, S.; Duncan, J.S.; Cross, J.H. *Epilepsia*, **2003**, *44*, 986-987.
6. Sterrett, S.P.; Penniston, K.L.; Wolf, J.S.; Nakada, S.Y. *Urology,* **2008**, *72*, 278-281.
7. Supuran, C.T. *Roum. Chem. Quart. Rev.* **1993,** *1,* 77-116.
8. Supuran, C.T.; Scozzafava, A. *J. Enzyme Inhib.* **1997,** *12,* 37-51.
9. Mincione, G.; Scozzafava, A.; Supuran, C.T. *Met.-Based Drugs* **1997,** *4,* 27-34.
10. Brezeanu, M.; Olar, R.; Manole, G.; Supuran, C.T. *Rev. Roum. Chim.* **1992**, *37*, 425-431.
11. Alzuet, G.; Casanova, G.; Ramirez, J.A.; Borrás, J.; Carugo, O. *J. Inorg. Biochem.* **1995**, *57*, 219-234.
12. Thimmaiah, K.N.; Chandrappa, G.T.; Lloyd, W.D.; Parkanyi, C. *Inorg. Chim. Acta* 1985, *107*, 1.
13. Ferrer, S.; Jiménez, A.; Borrás, J. *Inorg. Chim. Acta* **1987,** *129,* 103-106.
14. Ferrer, S.; Hasnoot, J.G.; de Graaf, R.A.G.; Reedijk, J., Borrás, J. *Inorg. Chim. Acta* **1992,** *192,* 129-138.
15. Ferrer, S.; Borrás, J.; Miratvilles, C.; Fuertes, A. *Inorg. Chem.* **1990,** *29,* 206-210.
16. Ferrer, S.; Borrás, J.; Miratvilles, C.; Fuertes, A. *Inorg. Chem.* **1989,** *28,* 160-163.
17. Ferrer, S.; Alzuet, G.; Borrás, J. *J. Inorg. Biochem.* **1989,** *37,* 163-174.
18. Ferrer, S.; Borrás, J.; Martin-Gil, J.; Martin-Gil, F.J. *Thermochim. Acta* **1989,** *153,* 205-220.
19. Çakır, S.; Biçer, E.; *Bioelectrochem.* **2005,** *67,* 75-80.
20. Çakır, S.; Bulut, I.; Biçer, E.; Çakır, O. *J. Coord. Chem.* **2003**, *56,* 511-521.
21. King, E.J. *The International Encyclopedia of Physical Chemistry and Chemical Physics*, Pergamon Press, Oxford, Vol. 4, 1965.
22. Smyth M.R.; Smyth, W. F. *The Analyst* **1978,** *103,* 538-
23. De Balugera, Z.G.; Goicolea, M.A.; Barrio, R.J. *J. Pharm.Biomed. Anal.* **1994,** *12,* 883-868.
24. Bard, A.J; Faulkner, L.R. *Electrochemical Methods, Fundamentals and Applications,* Wiley, New York, 1980.
25. Crow, D.R. *Polarography of Metal Complexes,*Academic Press, New York, 1969.
26. Gonçalves, M. L.S.; Sigg, L. *Electroanalysis* **1991,** *3,* 553 (1991).
27. Ferrer, S.; Borrás, J. *J. Inorg. Biochem.* **1990,** *39*, 297-306.
28. Chufán, E.E.; Pedregosa, J.C.; Ferrer, S.; Borrás, J. *Vibr. Spectrosc.* **1999,** *20*, 35-
29. Israel, Y.; Meites, L. Vanadium, in: Bard, A.J.; Lund, H. (Eds.), *Encyclopedia of Electrochemistry of The Elements,* Marcel Dekker, New York, 1973.
30. Xu, M.; Song, J.; Li, N.; Zhao, C. *J. Electroanal. Chem.* **2003,** *553,* 163-168.
31. Urbanska, J.; Kozlowski, H. *J. Coord. Chem.* **1997,** *42*, 197-205.
32. Çakır, S.; Bulut, I.; Biçer, E.; Coşkun E.; Çakır, O. *J. Electroanal. Chem.* **1999**, *511*, 94-100.

33. Alzuet, G.; Ferrer, S.; Borrás, J. *J. Inorg. Biochem.* **1991,** *42*, 79-86.

34. Hathaway, B.J; in: Wilkinson, G. (Ed.), *Comprehensive Coordination Chemistry*, Pergamon Press, Oxford, Vol.5, 1987.

35. Jubert, A.H.; Gonzalez-Baro, A.C.; Pis-Diez, R.; Baran, E.J. *J. Raman Spectrosc.* **1992,** *23*, 273-279.

36. Pal, S.; Radhika, K.R.; Pal, S. *Z. Anorg. Allg. Chem.* **2001,** *627*, 1631-1637.

37. Anthonysamy, A.; Salasubramanian, S. *Inorg. Chem. Chem.* **2005,** *8*, 908-911.