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# Determination of cadmium by differential pulse adsorptive stripping voltammetry

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**Abstract**

A study of the adsorptive stripping voltammetry of cadmium on a mercury drop electrode is reported in which 2-mercapto-5-phenil-ammino-1,3,4-thiadiazole (MPATD), synthesized at home has been used as a chelating agent. The most suitable operating conditions and parameters such as buffer, pH, deposition potential, deposition time, ligand concentration, scan rate and others were selected and the determination of cadmium from aqueous solutions using the standard additions method was possible. As validation criteria, the linearity and range, repeatability of the signal, repeatability of the concentration and accuracy were investigated. A limit of detection of $4.67 \times 10^{-10}$ M and a limit of quantification of $1.55 \times 10^{-9}$ M were achieved. The interference of other metals and organic substances was studied. Concerning a possible catalytic effect, no one was found. The method was designed in order to determine Cd from biological samples. © 2000 Elsevier Science B.V. All rights reserved.

*Keywords:* Cadmium; 2-Mercapto-5-phenil-ammino-1,3,4-thiadiazole; Accumulation cathodic voltammetry

## 1. Introduction

Cadmium occurs widely in nature in close association with zinc. Substantial amounts of cadmium are continuously added to soil, water and air as a consequence of human pollution. The cadmium inhaled from the air is in most circumstances insignificant (0.02 μg $day^{-1}$) compared with that ingested with food. The highest Cd concentrations are found in rice, wheat, oyster, mussels and kidney cortex of animals [1].

Cadmium is of great toxicological interest due to its unusually long half life and accumulation in soft tissues, chiefly in kidneys and liver in association with cadmium binding proteins. The measurement of cadmium is becoming more common in clinical and toxicology laboratories.

There are numerous methods that can determine cadmium at the ppb level in a variety of samples, e.g. graphite furnace atomic absorption spectrometry (GFAAS), direct coupled flame atomic absorption spectrometry (FAAS), neutron activation analysis (NAA) or X-ray fluorescence

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analysis [1,2]. In most of these techniques the analyte must be in solution, thus requiring a previous digestion of the organic matrix (that increases the risk of sample contamination and/or loss of analyte).

GFAAS is by far the most commonly used method for Cd determination in biological samples due to its low detection limit, and high sampling rate [2]. In the last few years, electroanalytical techniques, particularly adsorptive stripping voltammetry (AdSV) has attracted considerable attention for the determination of trace metals [3,4], as it combines low cost of instrumentation and maintenance with good accuracy and precision, and excellent sensitivity. In this technique, the analyzed metal is preconcentrated 'in situ' by the adsorption of its complex with an appropriate ligand onto the working electrode and subsequently stripped during the cathodic voltammetric scan. AdSV sensitivity and selectivity can be further improved by exploiting catalytic effects, or by developing new ligands, with high complexation capacity. The lower sampling rate of stripping voltammetry compared with GFAAS is overwhelmed by its ability for speciation studies and multielemental analysis.

It has been described the adsorptive collection of cadmium complexes with ligands such as oxine [5,6], 1-(2-pyridylazo)-2,7-dihydroxynaphthalene [7], calcein blue [8], glyoxylic acid thiosemicarbazide [9] ω-mercaptocarboxylic acids [10] or 2,5-dimercapto-1,3,4-thiadiazole [11] on the working electrode, followed by the voltammetric measurement of the adsorbed complex.

In the present study, a new ligand, 2-mercapto-5-phenil-ammino-1,3,4-thiadiazole (MPATD), synthesized by cyclization of disubstituted dithiourea, is investigated for the adsorptive cathodic voltammetric determination of cadmium from aqueous solutions using the hanging-mercury-drop electrode (HMDE) and a differential-pulse (DP) modulation of the potential to increase the sensitivity.

The complexing properties of this ligand containing S and N donors, have been studied during the last four decades in our department by gravimetric ($Pb^{2+}$, $Cu^{2+}$, $Hg^{2+}$, $Ag^{+}$, $Tl^{+}$) [12,13],photometric ($Bi^{3+}$, $Ni^{2+}$, $Pd^{2+}$) [12,14], enthalpymetric [15] conductimetric and potentiometric ($Ag^{+}$, $Hg^{2+}$, $Pb^{2+}$, $Cd^{2+}$) [13,16–18] methods. Lead, cadmium, copper and mercury traces were preconcentrated by solid-phase extraction using MPATD impregnated silicagel [19]. The voltammetric behaviour of MPATD in aqueous solution was studied at the carbon paste electrode [20].

In the AdSV procedure developed in this paper the MPATD–Cd complex showed good adsorption onto the HMDE, leading to a detection limit $L_d$ of $Cd^{2+}$ at the $10^{-10}$ M level (60 s accumulation time), better than that obtained with the most sensitive ligands cited. Thus, oxine provided a $L_d$ of $1 \times 10^{-10}$ M after 5 min accumulation [5] and 2,5-dimercapto-1,3,4-thiadiazole allowed a limit of quantification $L_q$ of $4.4 \times 10^{-9}$ M after 2 min accumulation ($L_d$ not given) [11].

## 2. Experimental

### 2.1. Apparatus

Voltammograms were registered with an Autolab PSTAT10 potentiostat (Eco-Chemie) connected to a Metrohm 663 VA electrodic stand used in the HMDE mode. The mercury was triple-distilled and the medium drop size was selected to maintain a compromise between well-shaped peaks and maximum peak heights. The cell also included a saturated calomel reference electrode (SCE) and a platinum rod as auxiliary electrode. Oxygen was expelled by purging with water-saturated nitrogen at 1 atm. The potentiostat, the stirrer (a rotating Teflon rod) and the purging system were controlled by an IBM PC-compatible computer using the GPES 4.4 software (from Eco Chemie). A Metrohm 654 pH meter using a combined glass electrode, a Sartorius electronic analytical balance, automated micropipettes Pipetman Gilson and Sterilin flasks were also employed.

### 2.2. Reagents

2-Mercapto-5-phenil-ammino-1,3,4-thiadiazole was prepared, crystallized and purified (m.p. 215–

216°C) in our laboratory using analytical-grade chemicals (Merck). The structure of the compound was confirmed by elemental analysis, IR and NMR spectroscopy. Its stability was found to be good in solid phase, protected from light. However, its purity was checked before use in this work by mass spectrometry. A stock solution of $10^{-2}$ M MPATD in 60% (v/v) ethanol was prepared weekly and kept at 4°C, in darkness, to avoid photoxydation. Prior measurement, the appropriate volume of ligand was pipetted into the voltammetric cell.

Stock solutions of cadmium (II) and interfering cations were prepared by dilution of the respective 1000 ppm AAS standards (Merck).

Three buffer solutions of different pH values were used in this study: (1) 1 M acetate buffers of pH ranging from 4.0 to 6.0 were prepared by adding the appropriate volumes of 1 M HCl to 1 M sodium acetate. Two hundred μl of these buffers were transferred into the voltammetric cell yielding a final concentration of $10^{-2}$ M. (2) 1 M *N*-hydroxyethyl-piperazine-*N*′-2-ethanesulphonic acid (HEPES) of pH values between 6.5 and 8.5 were prepared by adjusting the 1 M HEPES aqueous solution pH with the necessary amount of 1 M NaOH. A $10^{-2}$ M final concentration was used. (3) $10^{-2}$ M Tris–hydroxymethyl-amminomethane (Tris)/sodium maleate solutions (pH 5.1–7.0) were prepared by mixing 25 ml of a solution containing 0.2 M Tris and 0.2 M maleic acid with the adequate volumes of 0.2 M NaOH and diluting to 1000 ml.

Water purified in a Milli-Q water purification system (Millipore) was used for preparation of solutions and for rinsing the voltammetric cell. All chemicals were of analytical grade and used without further purification.

### 2.3. Procedure

Twenty ml of Milli-Q water were pipetted into the voltammetric cell and the pH adjusted to 6.0 by addition of 200 μl of 1 M acetate buffer. Then, 200 μl of $10^{-2}$ M MPATD were added, giving a final concentration of $10^{-4}$ M. The solution was purged with water-saturated nitrogen for 5–10 min in the first cycle and 5 s for each successive cycle. The preconcentration (adsorption) potential (usually $-0.7$ V) was applied for 60 s to a fresh mercury drop while the solution was stirred. Then, the stirring was stopped and the potential set to $-0.3$ V for a period of 10 s (equilibration time). Thereafter, the potential was scanned toward more negative values using differential pulse (DP) modulation (modulation time, 40 ms; modulation amplitude, 50 mV; interval time, 0.2 s and potential step, 5 mV, resulting in a scan rate of 25 mV $s^{-1}$). Each scan was repeated three times with a new drop for each analyzed solution and the mean of these voltammograms obtained. A cadmium-stripping peak was registered at about $-0.64$ V and its current used as a measure of cadmium concentration. The standard additions method was used (four additions) to calibrate the AdSV sensitivity and to check linearity of response. All experiments were carried out at room temperature.

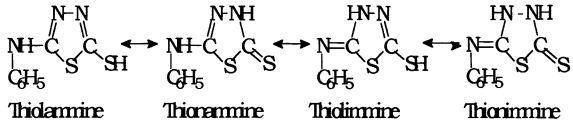



Fig. 1. MPATD chemical structure and tautomeric forms.

## 3. Results and discussion

### 3.1. Mechanism of the electrode reaction

The possible mechanisms of metal preconcentration on the electrode–solution interface in AdSV, via complex formation, were given by Paneli et al. [4]. According to these authors, it seems that the presence of S donors in the ligand molecule favours the chemisorption on the Hg electrode, while the presence of π-electrons increases the adsorption process.

MPATD is a weakly acidic heterocyclic compound ($pK_a = 8.04–8.20$) [21], that can exist in more tautomeric forms, depending on the pH of the solution (Fig. 1). As shown in Fig. 2 (solid line), a lot of cathodic peaks were obtained in $10^{-2}$ M pH 6.0 acetate buffer, over a wide potential range, as a consequence of the reduction of the coexisting tautomeric forms and of some pos-

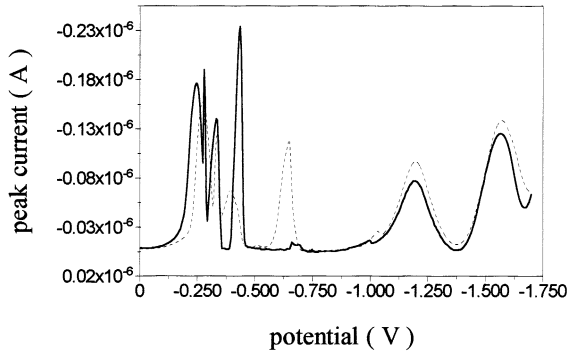



Fig. 2. DP cathodic stripping voltammograms of $10^{-4}$ M MPATD in the absence of $Cd^{2+}$ (solid line) and in the presence of $3.26 \times 10^{-7}$ M $Cd^{2+}$ (broken line) in $10^{-2}$ M acetate buffer pH 6.0; accumulation at $-0.70$ V for 60 s; equilibration time 10 s; scan rate 25 mV $s^{-1}$.

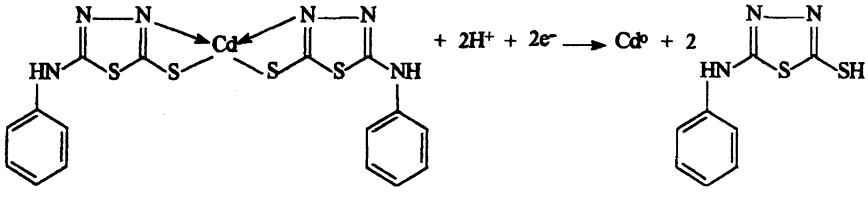
sible mercury thiolates [22]. The reduction mechanism of MPATD is still to be studied.

In the presence of cadmium ions (Fig. 2, broken line) a well-defined peak appeared at $-0.64$ V, while the MPATD peak in its immediate vicinity ($E = -0.435$ V) decreased strongly. The higher the cadmium concentration, the smaller the incriminated ligand peak height, indicating that a stable chelate complex forms, involving most probably both the cyclic N and sulphydryl group of the ligand. The most probable structure of the cadmium complex is 1:2 as indicated in the reaction (1). It can be assumed that at $-0.435$ V occurs the reduction of the thionic group of the non-complexed MPATD. In the presence of $Cd^{2+}$ the thion–thiolic balance in the solution, as well as at the electrode surface, is shifted toward the thiolic form due to the complexation, so that the thionic form ratio diminish, fact that explain the decrease of its peak. By applying a negative-going potential scan the reduction of the metal centre in the adsorbed complex takes place, giving $Cd^{o}$ that is amalgamated and 'dissolves' into the HMDE and 'free' thiol, according to reaction (1).

### 3.2. Effect of various parameters on the DPAdSV sensitivity for Cd(II) using MPATD

#### 3.2.1. Influence of pH

Owing to both the pH dependent thion–thiolic MPATD balance (as mentioned above) and the competition between proton and $Cd^{2+}$ for the binding sites in the ligand molecule, the pH is a very important parameter. Its influence on the stripping peak of Cd was investigated in the range 4–8.5 for a solution containing 50 μM MPATD and 0.30 μM $Cd^{2+}$ in 10 mM acetate, HEPES or TRIS buffers (see Fig. 3). Maximum peak current was achieved in HEPES buffer at pH 7.0, this value offering a compromise between the complexing sulphydryl group ratio and the hydrolysis of the metal ion that occur in alkaline medium. Cadmium yielded small peaks in TRIS buffer due to its competitive complexation in solution by maleic acid. The repeatability of the cadmium peak in consecutive scans was higher in pH 6 acetate buffer, due to a better stability of the complex and increased with decreasing pH. Moreover, the risk of contamination of the electrodic cell decreased with decreasing pH. The contamination is presumably due to both the amalgamated cadmium and the accumulated ligand since the later can only be completely removed by keeping the electrode in ethanol for 1–2 min, fact that proves a strong adsorption of the ligand and/or the metal complex. As it is shown in Fig. 3B, the peak potentials of both cadmium and the nearest ligand peak shifted towards more negative values with increasing pH, but higher peak resolution was obtained in acidic solutions. Taking into account the reasons above mentioned and also its lower cost, acetate buffer of pH 6 was selected for subsequent experiments. Under these conditions, the cadmium peak occurred at $-0.632$ V and was stable for about 1 h. In addition, the interference




(1)

from zinc ions was considerably smaller than at pH 7 in HEPES buffer.

### 3.2.2. Effect of accumulation parameters

The dependence of the cadmium peak current on the accumulation potential was examined over the range from 0 to −1.20 V (Fig. 4A). It was found that the peak height was almost constant between −0.40 and −0.8 V. The value −0.70 V, providing the maximum peak height, was selected for cadmium accumulation. At this potential Cd(II) is reduced to Cd(0) and amalgamated into the Hg drop, but it is likely (in view of the adsorptive mechanism proposed) that oxidation of Cd(0) occurs at the initial potential of the voltammetric scan (−0.35 V, usually) during the equilibration period. Thus $Cd^{2+}$ diffuses out of the Hg drop and is retained at its surface by complexation with the ligand in the adsorption layer, where it is again

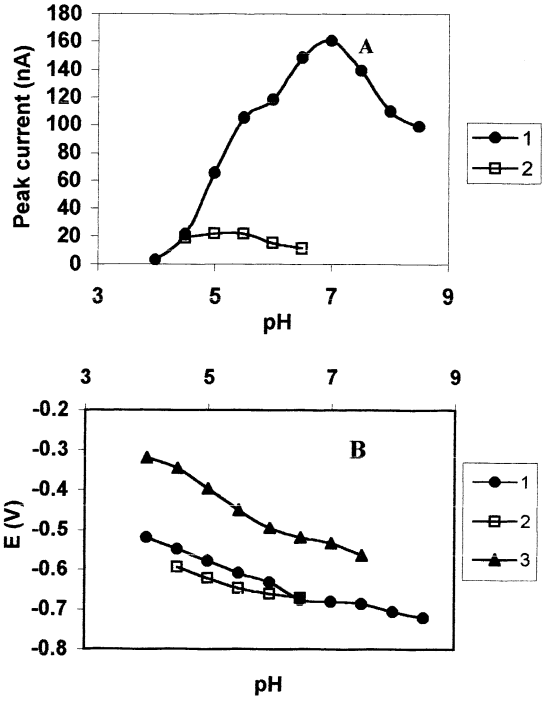



Fig. 3. Effect of pH on (A) peak current and (B) peak potential of 0.30 μM Cd(II) and 50 μM MPATD in 10 mM buffer: (1) pH 4.0–6.0 acetate and pH 6.5–8.5 HEPES buffers, (2) pH 5.0–7.0 Tris buffer. Curve 3 refers to free ligand peak in acetate and HEPES buffers. Accumulation at −0.50 V for 60 s; scan rate 25 mV $s^{-1}$.

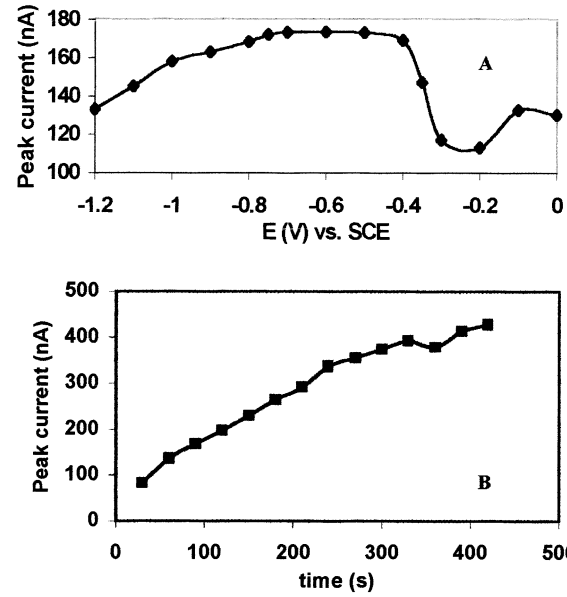



Fig. 4. Effect of accumulation potential (A) and accumulation time (B) on the AdSV sensitivity for 0.30 μM cadmium and 50 μM MPATD. Other conditions as in Fig. 2.

reduced during the cathodic sweep. Nevertheless, it seems that this mechanism provides only a very small improvement in the peak height. Therefore, any accumulation potential, ranging from −0.4 to −0.8 V could be also used.

Variation of the accumulation time showed that the peak current increased linearly with the accumulation time, gradually levelling off at periods longer than 300 s (Fig. 4B) presumably due to saturation of the electrode surface with free ligand. An adsorption time of 60 s was used throughout this work as it combines good sensitivity and relatively short analysis time. However, the sensitivity can be further increased by extending the accumulation period.

### 3.2.3. Influence of ligand concentration

As expected, MPATD concentration has a great influence on the sensitivity of Cd determination, a non-linear dependence being noted (Fig. 5). The variation of cadmium peak current (curve 1), but also the variation of the free ligand peak that was found to be involved in the cadmium complexation (curve 2) were investigated. The MPATD concentration ranged from 10 to 130 μM. According as

cadmium peak increases, the free ligand peak decreases, the curve 2 being the mirror image of the curve 1. The greatest variation in the peak height for both the Cd and the ligand occurs between 20 and 30 μM MPATD. Then, the Cd peak height increases gradually, simultaneously with the ligand peak decrease, up to 100 μM ligand and then levels off. At concentrations higher than 120 μM MPATD the both peaks diminish as a consequence of a full electrode surface coverage. Consequently, an optimum MPATD concentration of 100 μM was selected for further experiments. The potential of the cadmium peak shifted 15 mV in the cathodic direction when the MPATD concentration was increased from 10 to 30 μM, remaining constant above 30 μM ($E = -0.632$ V) due to the complex stabilization. This phenomenon was observed in other AdSV procedures, too [23].

### 3.2.4. Influence of scan initial potential

A marked gain in Cd sensitivity was obtained when the stripping voltammogram was scanned from a potential as close as possible to the cadmium peak potential. In order to register also the free ligand peak (at around $-0.40$ V), scans were recorded from an initial potential of $-0.30$ V.

The optimum conditions for the determination of cadmium can be then summarized: pH 6 obtained with $10^{-2}$ M acetate buffer; $10^{-4}$ M MPATD; 60 s accumulation onto the HMDE at $-0.7$ V. The rest of experimental variables were used as described in section 2.

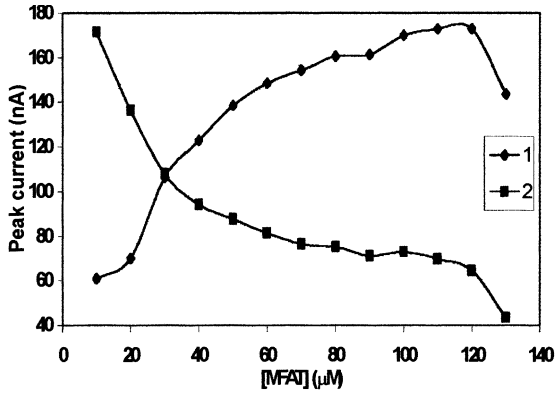



Fig. 5. Effect of MPATD concentration on the peak current of 0.30 μM cadmium and on the peak current of free MPATD (curves 1 and 2, respectively). Experimental conditions as in Fig. 2.

### 3.3. Performance characteristics of the procedure

The linearity was evaluated by increasing the concentration of cadmium up to $4.28 \times 10^{-6}$ M. The calibration plot obtained in the optimized conditions was linear over the range $1.09 \times 10^{-9}$–$1.3 \times 10^{-6}$ M $Cd^{2+}$ with a correlation coefficient of 0.9923. The best linearity (correlation coefficient 0.9964) was achieved in the range $1.09 \times 10^{-9}$–$3.26 \times 10^{-7}$ M $Cd^{2+}$, the equation of the straight line being $I_p$ (nA) $= 2.96 + 4 \times 10^8 C$ (M). As the cadmium concentration increased, the free ligand peak potential shifted toward less negative values (from $-0.427$ to $-0.359$ V) and disappeared completely at cadmium concentrations higher than $5.43 \times 10^{-7}$ M $Cd^{2+}$.

To establish the detection limit of the procedure a solution containing 1.63 nM $Cd^{2+}$ was repeatedly measured ($n = 8$, RSD = 9.72%) following 60 s accumulation time. The $L_d$, calculated according to Miller and Miller [24] as $3s/m$, where $s$ is S.D. and $m$ the slope of the calibration plot, was found to be 0.46 nM. The $L_q$ was calculated as $10s/m$ and resulted in 1.55 nM. By increasing the accumulation period these values can be further reduced.

The adsorptive accumulation of the cadmium–MPATD complex under the optimized conditions results in reproducible peak currents. Sixteen successive measurements of 0.30 μM cadmium yielded a mean peak current of $98.74 \pm 0.76$ nA and a relative standard deviation (RSD) of 1.46%. The analytical precision (expressed as repeatability) was evaluated by measuring the concentration of seven aliquots of 25 μg $l^{-1}$ cadmium giving an average cadmium concentration of $23.11 \pm 0.99$ μg $l^{-1}$ (RSD 4.64%).

To assess the accuracy of the method, three levels of cadmium in aqueous solution were tested (Table 1) the recoveries being satisfactory.

### 3.4. Selectivity of the method

#### 3.4.1. Interference by other metals

The influence of concomitant ions that are

Table 1
Cadmium determination from aqueous solutions

| Sample concentration (M) | Recovery[a] (%) | R.S.D.% ($n=3$) | Confidence interval ($n=9$; $P=95\%$) (%) | R.S.D.% ($n=9$) |
|---|---|---|---|---|
| $5.55\times10^{-9}$ | 109.50 | 5.30 | | |
| $1.13\times10^{-7}$ | 95.78 | 5.16 | $100.42\pm6.13$[b] | 7.93 |
| $2.27\times10^{-7}$ | 95.97 | 3.1 | | |

[a] Each of these values is the average of three determinations by standard addition method.
[b] $t(s/\sqrt{n})$.

Table 2
Influence of concomitant ions on the peak current of $3.3\times10^{-7}$ M cadmium ($E_p=-0.632$ V) and 50 μM MPATD in the optimized experimental conditions

| Ion | Concentration of concomitant ion (M) | Cd peak height ratio (%) | Peak potential of concomitant ion (V) |
|---|---|---|---|
| $Cu^{2+}$ | $1\times10^{-8}$ | 94.28 | – |
| | $5\times10^{-7}$ | 84.69 | −0.368 |
| $Zn^{2+}$ | $1\times10^{-6}$ | 97.92 | −0.930 |
| | $1\times10^{-5}$ | 96.77 | −0.935 |
| $Co^{2+}$ | $5\times10^{-7}$ | 98.79 | −1.081 |
| | $1\times10^{-6}$ | 94.96 | −1.052 |
| $Ni^{2+}$ | $5\times10^{-7}$ | 93.02 | −0.928 |
| | $1\times10^{-6}$ | 78.85 | −0.845 |
| $Pb^{2+}$ | $4.5\times10^{-7}$ | 118.71 | −0.449 |
| | $1\times10^{-6}$ | 132.15 | −0.449 |
| $Hg^{2+}$ | $1\times10^{-7}$ | 93.37 | – |
| | $4.6\times10^{-7}$ | 73.43 | – |
| $Bi^{3+}$ | $6\times10^{-8}$ | 117.16 | – |
| | $4.7\times10^{-7}$ | 170.64 | – |

known to form complexes with MPATD such as $Cu^{2+}$, $Zn^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Pb^{2+}$, $Hg^{2+}$ and $Bi^{3+}$ was investigated. Measurements of Cd peak current were generally carried out for concomitant ions at concentrations equal and up to 100 times of that of cadmium ($3.3\times10^{-7}$ M). As shown in the Table 2, MPATD offers poor selectivity in both metal complexation and complex adsorption on the Hg electrode. At the levels of concentration studied, all investigated ions significantly modify the cadmium peak height, except $Zn^{2+}$ and $Co^{2+}$. Distinct peaks appear in the case of some studied metals (especially $Zn^{2+}$ and $Ni^{2+}$) but the peak of cadmium is well separated from all of them. The resolution being so good, the simultaneous determination of $Zn^{2+}$ and $Cd^{2+}$ in particular experimental conditions could be possible.

### *3.4.2. Interference by organic complexing substances*

Many proteins and enzymes containing thiolic groups that are present in the biological materials can also interfere with the determination of trace cadmium by DPAdSV due to competition with the added ligand, MPATD. This competitive effect was modeled by addition of EDTA, as shown in Fig. 6. The complex of Cd(II) with EDTA forms in the solution and does not adsorb onto the HMDE. At EDTA concentrations 1000-fold lower than that of MPATD the peak of cadmium starts to decrease greatly and is completely suppressed at EDTA concentration equal to that of

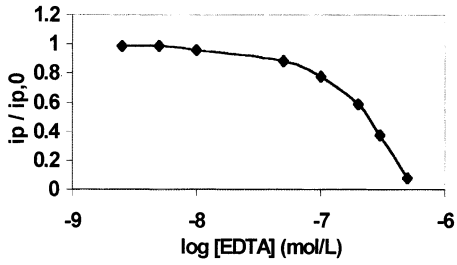



Fig. 6. The influence of competitive complexing organic ligands (modelled by EDTA) on the relative peak height ($i_p/i_{p,o}$) of 0.30 μM $Cd^{2+}$, under the optimized conditions.

$Cd^{2+}$. This indicates a relatively low stability of the complex cadmium–MPATD and the necessity to destroy the organic substances prior to analysis.

## 4. Conclusions

The aim of this work was to investigate a new ligand containing sulphur atoms, 2-mercapto-5-phenil-ammino-1,3,4-thiadiazole and to set up a procedure for the determination of cadmium ions by the DPAdSV technique. MPATD was found to have an interesting behaviour at the HMDE and the mechanism of its reduction is still to be studied. The cadmium complex is accumulated onto the working electrode and then reduced at about −0.64 V. The sensitivity of the proposed procedure is superior to that provided by other ligands and hold promise for the application in the analysis of biological samples. The method is rapid and capable of application to many other elements. The simultaneous determination of cadmium and zinc is anticipated.

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## References

[1] C.J. Menendez-Botet, M.K. Schwartz, Anal. Chem. 63 (1991) 196R.
[2] R.F.M. Herber, in: H.G. Seiler, A. Sigel, H. Sigel (Eds.), Handbook on Metals in Clinical and Analytical Chemistry, Marcel Dekker, New York, 1994, pp. 283–297.
[3] C.M.G. van den Berg, Anal. Chim. Acta 250 (1991) 265–276.
[4] M.G. Paneli, A. Voulgaropoulos, Electroanalysis 5 (1993) 355–373.
[5] C.M.G. van den Berg, J. Electroanal. Chem. 215 (1986) 111.
[6] M. Strozik, W.W. Kubiak, Z. Kowalski, Chem. Anal. 40 (1995) 1–12.
[7] Z.Q. Zhang, S.Z. Chen, H.M. Lin, H. Zhang, Anal. Chim. Acta 272 (1993) 227–232.
[8] K. Yokoi, M. Mizumachi, T. Koide, Anal. Sci. 11 (1995) 257–260.
[9] L.J. Zhou, Q.C. Zhu, J.M. You, H.N. Li, Feuxi Huaxue 23 (1995) 243.
[10] I. Turyan, D. Mandler, Anal. Chem. 66 (1994) 58–63.
[11] C. Li, B.D. James, J. Rumble, R.J. Magu, Mikrochim. Acta 111 (1988) 175–182.
[12] E. Popper, L. Popa, V. Junie, L. Roman, Rev. Chim. (Bucuresti) 11 (1960) 44–48.
[13] L. Roman, E. Florean, M. Echim-Grosu, E. Dorda, Rev. Roumaine Chim. 23 (1978) 929–933.
[14] L. Roman, R. Craciuneanu, E. Popper, Mikrochim. Acta (1968) 660–663
[15] E. Popper, L. Roman, P. Marcu, Talanta 11 (1964) 515–521.
[16] E. Popper, I. Pitea, Farmacia 16 (1968) 193–198.
[17] E. Popper, L. Roman, P. Marcu, M. Bojita, M. Serban, Rev. Roumaine Chim. 16 (1971) 569–575.
[18] L. Roman, M. Serban, V. Gug, Rev. Roumaime Chim. 29 (1984) 211–217.
[19] L. Roman, E. Florean, R. Sandulescu, S. Mirel, J. Pharm. Biomed. Anal. 14 (1996) 1003–1006.
[20] R. Sandulescu, I. Marian, S. Mirel, R. Oprean, L. Roman, J. Pharm. Biomed. Anal. 18 (1998) 75–81.
[21] L. Roman, S. Mirel, E. Florean, R. Oprean, J. Pharm. Biomed. Anal. 18 (1998) 137–144.
[22] F.G. Banica, A.G. Fogg, J.C. Moreira, Talanta 42 (1995) 227–234.
[23] M. Vega, C.M.G. van den Berg, Anal. Chem. 69 (1997) 874–881.
[24] J.C. Miller, J.N. Miller, Statistics for Analytical Chemistry, Ellis Horwood, Chichester, UK, 1984.