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Voltammetric Study of Cd^{2+} Complexation with some Compounds of Garlic

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Abstract

The complexation of Cd^{2+} by diallyl disulfide (DADS) and diallyl sulfide (DAS) has been studied by differential pulse voltammetry. Stability constants, (log β), of the 1:1 (PbL) and 1:2 (PbL2) complexes, where L = ligand, were found to be in the range of ca. 5.8 - 6.2 and 9.6 -10.6, respectively. Complex formation is accompanied with a significant decrease in the peak current and the shift of the Cd^{2+}/Cd half-wave potential to a higher one upon the addition of the sulfur containing ligands (L). The formation of 1:1 and 1:2 complexes, i.e., CdL^{2+} and $CdL2^{2+}$ was observed in the case of the two ligands. The consecutive formation constants of labile lead complexes with DADS and DAS were determined at 298K by the method of DeFord and Hume. Apparently due to the large size of the cadmium ion, steric hindrance caused by the greater steric bulk of DADS compared to that of DAS have little or no effects on the formation constants, so that very similar values were obtained in the case of the two ligands. Also, the possible participation of C=C double bonds in coordination with the metal center in the case of DADS appears to compensate for the steric effects caused by the larger size of this ligand. In agreement with the Jorgensen principle of symbiosis, the second formation constants were found to be approximately six orders of magnitude greater than the first ones.

Keywords: *Cadmium (II) - DADS and DAS complexes, Stability constant, DeFord-Hume methodology.*

Introduction

Cadmium, (Cd), is a highly toxic metal found in the earth's crust [1, 2]. This metal accumulates in body and proved to be a multitarget toxicant causing damage to many organs, such as liver, kidney, lung, brain, testis, bone, placenta, etc.

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[3]. Cadmium has an extremely long biological half-life (10–30years) that essentially makes it a cumulative toxin[4, 5]. Based on reports of the Agency for Research on Cancer, Cd has been classified as a group I carcinogen causing tumors in lung, liver, kidney and testis [6].

Chemopreventive agents have been used against the toxic effect of many compounds, including heavy metals. A range of vegetables, plants and synthetic compounds have been screened in order to ascertain whether they have potential in the prevention and cure of many diseases and conditions [7,8]. As one plant studied extensively, garlic (*Allium sativum*), has been used since ancient times as a cure for many diseases [9]. It has antifungal, antithrombotic, antibacterial, antihypertensive, anti-carcinogenic and antioxidant properties [10].Garlic belongs to the family *Liliaceae* and has a higher concentration of sulfur compounds which yield the characteristic flavor and taste and are also responsible for the beneficial effects [11]. In this respect, garlic aids the liver in lowering the levels of heavy metal especially lead, cadmium and mercury [7]. When garlic is minced, or crushed, the allyl sulfur compounds are formed by enzymatic activity. These extracts are composed of allicin, water-soluble S-allylmercaptocysteine and S-allylcysteine, and oil-soluble diallyl disulfide (DADS), diallyltrisulfide and diallyl sulfide [12,13], and additionally, allicin also consists of DADS, diallyl sulfide (DAS), diallyltrisulfide (DTS) and sulfur dioxide [14]. Organosulfur compounds can adsorb on the surface of gold or silver electrodes through several chemisorption steps. Thiols and disulfides compounds can adsorb by an anodic oxidation process on the surface of Au and Ag [15].

The study of the binding of cadmium (II) to the organic sulfur compounds of garlic oil and extracts is especially of importance in the modeling of the inhibitory effects of garlic on the cadmium poisoning. In the Pearson hard and soft acid and base sense, cadmium ions are classified as soft and, hence, should form complexes with sulfur containing ligands due to the soft character of the sulfur atom [14,16]. The study of the binding of heavy metal ions by peptides and proteins is especially important for the understanding of many biological systems. Among the strategies that can be applied for this purpose, the use of potentiometric and spectroscopic techniques deserves especial attention, due to the ability of potentiometry to determine accurate values for the stability constants and due to the large variety of structural information that can be obtained from the different spectroscopies [17]. However, these techniques are limited by their low sensitivity, which makes their application impossible when a large concentration of the ligand cannot be reached (e.g. to prevent complex precipitation). In such situations, voltammetric techniques can be a suitable alternative [18,19], especially considering their high sensitivity and the strong dependence of the signals on the distribution of the metal species [20].

In electrochemical techniques the general approach to obtaining quantitative information is through the postulation of an electrochemical model and its mathematical solution followed by the fitting of the parameters of the model's equations to the experimental data. This general approach can be called hard modeling [21-23]. Some investigators have used hard modeling approaches for the study of complexation of heavy metals with different ligands in electrochemistry; cadmium binding by the C-terminal hexapeptide [24], Cd^{2+} and Pb^{2+} - binding to glycine [25], competitive complexation of β- and α-metallothionein domains with cadmium and zinc [26], Cd^{2+} complexation by the glutathione-fragment [27] are some examples that were studied by electrochemical techniques.

In this study, complexation of two organic sulfurs of garlic oil including DADS and DAS (Figure 1) [28] with cadmium (II) has been studied by differential pulse voltammetry (DPV) using gold electrode. The information on the metal complexation is provided from the fitting of the parameters of the model to the experimental data.

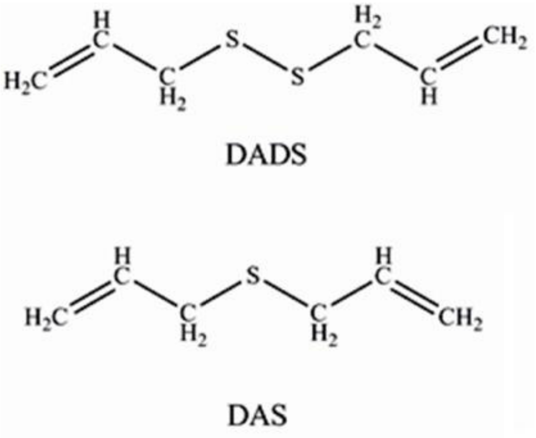

Figure 1. Organic sulfur compounds used in this study.

Experimental

Chemicals and instrumentation

Diallyl disulfide and diallyl sulfide, cadmium nitrate, sulfuric acid, acetic acid, sodium hydroxide and boric acid were of Merck or Sigma-Aldrich analytical grade. Stock solutions of the ligands (0.01 M of DADS, DMDS and DAS) was prepared by dissolving appropriate amount of them in 40 ml distilled methanol and diluting to the mark in a 100 mL calibrated flask with distilled water. Stock Cd(II) solution (0.03 M) was prepared by dissolving appropriate amount of $Cd(NO_3)_2.4H_2O$ in doubly distilled water.

Electrochemical experiments, (differential pulse voltammetry, DPV), were carried out using a computrace 757 VA from Metrohm. In all cases,a three-electrode system consisting of a gold electrode as the working electrode with diameter of 2 mm from Metrohm, a platinum wire counter electrode and an Ag/AgCl, KCl (3 M), reference electrode wereused.The gold electrode was abraded with a fine grade of furriery paper and polished to a mirror-like surface with 0.05 mm Al_2O_3 powder, and immersed in NaOH (0.2 M) then rinsed ultrasonically with water and ethanol for 3 min.All electrochemical measurements were carried out in a 12 mL cell.

Voltammetric measurements

Electrochemical measurements were performed in the solutions of acetate buffer pH = 5.5, with ionic strength of 0.10 mol/L. All the measurements were carried out in a glass cell at room temperature, (25°C), and the solutions were purged with nitrogen for at least 30 minutes prior to each experiment and the nitrogen atmosphere was maintained thereafter and DPV for each addition was recorded at a sweep rate of 0.1 V/s. The starting and ending potentials of all the titration experiments were from 0.25 V to -0.6 V vs. Ag/AgCl. Dialkyl disulfides are known to form the adsorption layer on gold electrode at negative potentials [29]. To solve this problem, after recording each voltammogram (at different ligand to metal molar ratios), the electrode surface was cleaned electrochemically by applying the potential of 1.5 V for 120 s. This potential is high enough for obtaining the reliably clean gold surfaces, as it was checked by obtaining the reproducible blank ground current. Less than 120 s of cleaning time, the electrode surface was not clean enough for electrochemical measurements. Each titration experiment was repeated at least four times. The experimental conditions for differential pulse voltammetry (DPV) were as follows: pulse amplitude 50 mV, pulse width 0.05 s and scan rate of 0.05 Vs^{-1}.The voltammograms were smoothed and converted into data matrices by means of internally written programs implemented in MATLAB.

Results and discussion

In the present study, the complex formation between Cd2+and DADS, DMDS and DAS has been studied by DPV. The electrochemical study of the complexation of thiol-containing ligands with cadmium ion was faced with difficulties caused by the high affinity of thiol-containing ligands, or their complexes, onto the surface of electrode. A simple voltammetric method was proposed for in situ and simultaneous cleaning of the electrode surface. According to the results, applying a high positive potential (+1.5 V for 120 s) can remove the organic sulfur compounds of garlic oil and their complexes from the surface of electrode after each recoeding voltammogram.

Optimization of conditions

The complexation of cadmium(II) with the used ligands in aqueous solution can be affected by a variety of factors and conditions such as the type of electrode, the buffer type, pH and initial concentration of metal ions which were considered in this study. Although electrodes such as mercury film, glassy carbon and carbon paste electrode were also checked for this purpose, it was verified that the changes in voltammograms during the titration were not enough for the evaluation of the stability constants and therefore a gold disk electrode was used as working electrode.

The effect of pH on the peak current was investigated by a set of DPV of the electrolyte containing 2.60×10^{-5}mol/L Cd^{2+}, while the solution pH was varied from 3 to 7. The current of signal of the voltammetric peak of Cd^{2+} increased with increasing pH from 3 to 5.5, and then decreased, which is a consequence of the formation of labile, cadmium hydroxide complexes. Also the peak potential of Cd^{2+} was nearly constant with increasing the pH up to 5.5 and subsequently shifted to lower potentials, (more negative potentials), with increasing pH. Hence, this pH,(pH = 5.5), was chosen for further experiments.

Figure 2 shows the set of voltammograms obtained by the successive addition of Cd^{2+} into the acetate buffer solution. It is observed from Figure 2, by increasing the concentration of cadmium ions, a splitting on the reduction potential of cadmium occurred. The Cd^{2+} reduction signal are split, which seems to indicate a two-step deposition process of Cd^{2+} on the Au-electrode surfaces. Such a behavior was also observed for Hg^{2+} ions on the surface of gold electrode [29].For this purpose, a concentration of 2.60×10^{-5}M Cd^{2+} in which there is only one peak in the voltammogram was chosen as initial concentration of metal ion inthe titration of the metal ion with the ligands.

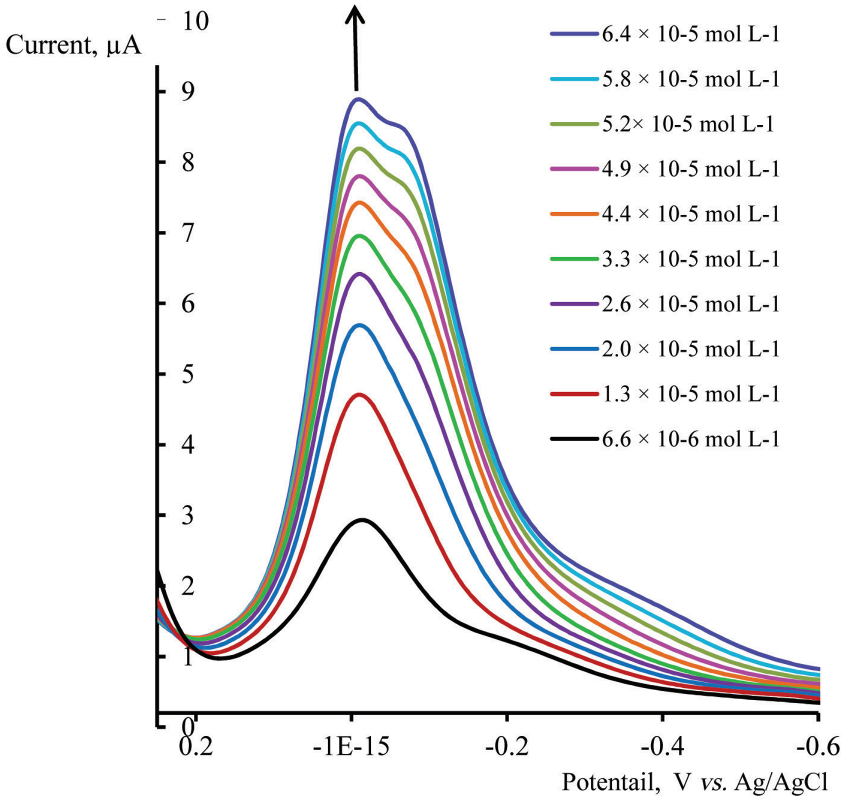

Figure 2. DP voltammograms recorded in 0.1 M acetate buffer (pH = 5.5±0.1) with increasing concentrations of Cd(II) ions.

Determination of the stability constants by fitting method

As Figure 3 shows, the increment in ligand concentration produces a shift of the peak potential towards more negative values. Also, the distribution diagram of Cd^{2+} by DADS, DMDS and DAS are shown in Figure 4. The basis for interpreting the DPV data was the well-known De Ford-Hume relation:

$$\Delta E\,(C_{Cd}) = E\,([L]) - E\,([L] \rightarrow 0) = (\frac{R}{2F})ln\,\alpha_0 \qquad (1)$$

Where E stands for a half-wave or a peak potential, whichever is appropriate, and α0 stands for the fraction of non-ligated cadmium. The ratio of the diffusion currents of a ligated and a non-ligated cadmium was omitted because it was not readily calculable from the DPV data and the Ep value has a greater effect on the calculated stability constants than the variation in the height of cadmium peak. In terms of Leden's function F0, the final mathematical model can be written as:

$$F_0 = \frac{1}{\alpha_0} = 1 + \beta_1[L] + \beta_2[L]^2 + \ldots \qquad (2)$$

If only one labile complex is present, the shift of the peak potential can be expressed as:

$$\Delta E_p = \frac{R \qquad (1+\beta_1[L]+\beta_2[L]^2+\ldots+\beta_n[L]^n)}{2F} \qquad (3)$$

where L stands for the ligand and βnare the corresponding cumulative stability constants [30].

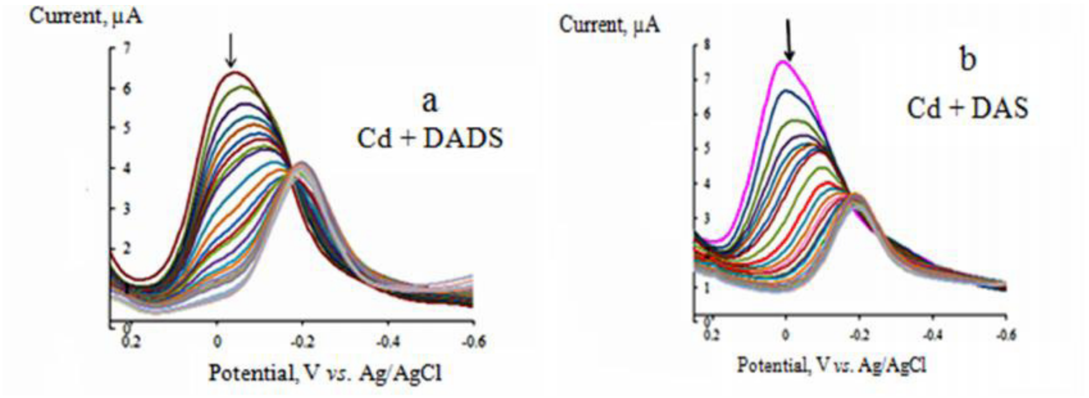

Figure 3. DPV obtained for titration system of Cd^{2+} 2.60×10^{-5} M solution with a) DADS, b) DAS in the presence of 0.1 M acetate buffer (pH = 5.5±0.1).

The complex formation equilibrium of the Cd2+ ion with DADS and DAS in dilute aqueous solution is assumed to be established by the consecutive two-step reactions:

$$M^{2+} + L = ML^{2+} \qquad (4)$$

$$ML^{2+} + L = ML_2^{2+} \qquad (5)$$

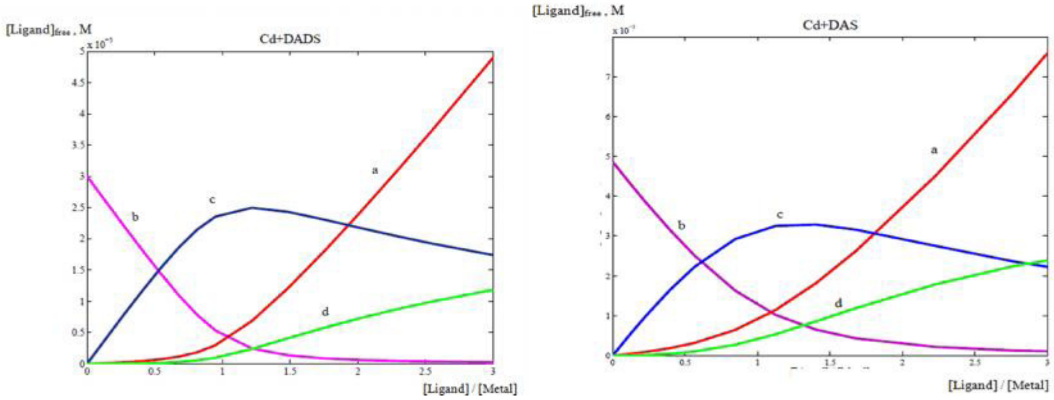

Figure 4. Distribution diagram of complexation of Cd^{2+} by DADS and DAS in presence of 0.1 M acetate buffer (pH = 5.5±0.1), Ligand a), Cd^{2+} b), ML^{2+} c), ML_2^{2+} d).

Computations of the stability constants, under the assumption of a series of mononuclear complexes (ML_n; n = 1, 2…) estimated by voltammetry, yielded the values of formation constants as follows: (DADS): log β_1 = 6.2±0.2 and log β_2 = 10.3±0.1 and (DAS) log β_1 = 5.8±0.0 and log β_2 = 9.6±0.2.All measurements were performed at pH = 5.5, where the formation of cadmium(II) hydroxide was negligible. Interestingly, the second formation constants are approximately four orders of magnitude greater than the first ones. This observation is in agreement with the Jorgensen principle of symbiosis with respect to hard and soft acid-base behavior [31]; this rule states that the presence of some soft ligands enhances the ability of the central atom to accept other soft ligands. Although the sulfur groups of the used ligands are most probably involved in coordination to the metal center, the involvement of double bonds in the optimized structure of the complexes of DADS and DAS cannot be excluded. Also, the comparable consecutive formation constants in the case of DADS in spite of the absence of C=C bonds in DAS, suggests that the Cd(II)-S bonds are probably the main interactions in the complexes. According to the obtained formation constants, inhibitory and treatment effects of garlic oil [32] on the cadmium poisoning may be quantitatively described based on the formation of the 1:1 and 1:2 complexes. As Figure 5 shows the dependence of reduction potential shifts (related to the potential without ligands) on ligands concentration.

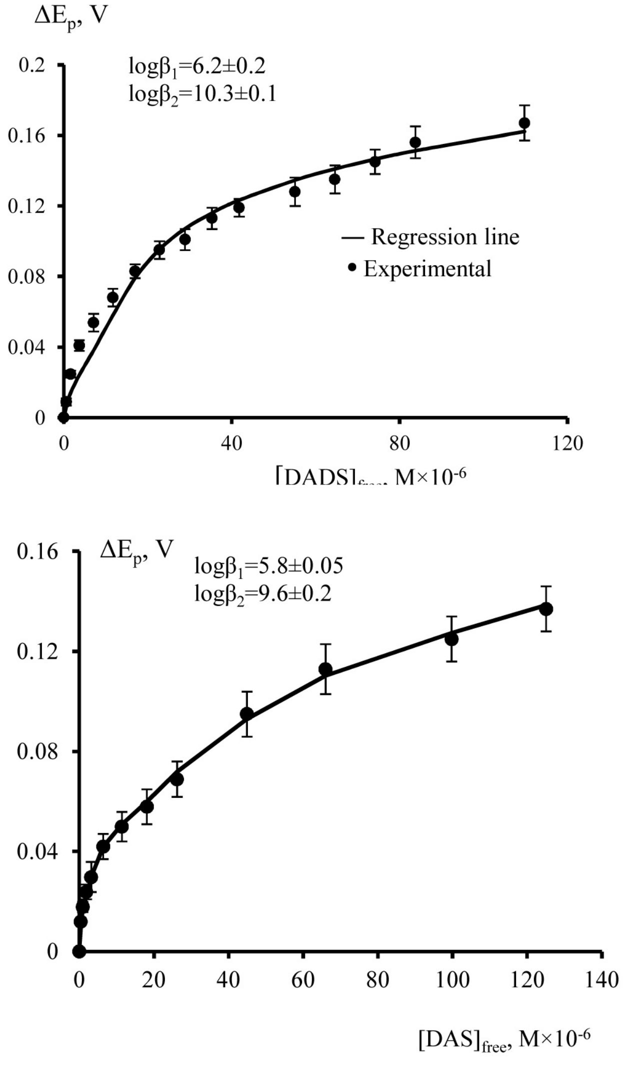

Figure 5. Dependence of the shift of the potential reduction of Cd^{2+} on DADS and DAS concentration presence of 0.1 M acetate buffer (pH = 5.5±0.1).

Conclusion

In this study, the formation of 1:1 and 1:2 complexes between cadmium(II) and diallyl disulfide (DADS) and diallyl sulfide (DAS) has been studied by differential pulse voltammetry. The effect of pH on the peak current was investigated by a set of DPV from 3 to 7. pH = 5.5 was chosen for further experiments to avoid metal hydroxide precipitation.

Accordingly, the inhibitory effects of DADS and DAS that are the main components of the garlic oil on the cadmium poisoning may be explained on the basis of formation of the 1:1 and 1:2 complexes between Cd(II) and the organosulfur compounds with stability constants (β) in the range of ca. $10^{5.8}$- $10^{6.2}$ and $10^{9.6}$-$10^{10.6}$. Apparently, due to the large size of Cd(II) ion, the greater steric bulk of DADS relative to DAS have little effects on the formation constants so that very similar formation constant values were obtained in the case of the two ligands. However, the involvement of C=C double bonds in coordination to metal centre in the case of DADS may also compensate the steric effects caused by the larger size of this ligand. In agreement with the Jorgensen principle of symbiosis, the second formation constants are approximately six orders of magnitude greater than the first ones. Furthermore, DADS has two sulfur groups in their structure that may explain their greater complexation constants with respect to that of DAS.

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