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Electrochemical study of gallium(III) with L-glutamine at the dropping mercury electrode

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Abstract Gallium complexes of L-glutamine have been studied polarographically in aqueous media. The reduction was found to be irreversible and diffusion controlled in the presence of 0.1 M KNO_3 and 0.002% Triton-x-100. The values of kinetic parameters, transfer coefficient (α_n), and formal rate constant ($k^0_{f,h}$) of the electrode reactions were calculated by Koutecky's method. The stability constants and composition of the gallium(III)-L-glutamine complexes were evaluated with the help of the Deford-Hume method. The values of stability constants of 1:1, 1:2, and 1:3 gallium(III)-L-glutamine complexes are 1.35, 6.5, and 1,350 at 30 °C, respectively. The values of thermodynamic parameters, the free energy of activation, the enthalpy of activation, and the entropy of activation have been determined at 30 °C. The formation of the metal complexes has been found to be non-spontaneous, endothermic in nature, and entropically favorable at higher temperature.

Keywords Amino acids · Metal complexes · Reductions · Polarographic · Irreversible · Kinetic Parameters

Introduction

Amino acids are well known for their tendency to form complexes with metals, have great significance in biological and pharmaceutical fields, and are directly involved in all the metabolic, enzymatic reactions. The complexes of amino acids with metals are used in cancer therapy, pharmacy, and industry [1, 2]. L-Amino acids are biologically active, with considerable interest focused on their metal complexes [3]. They have good chelating ability with metal ions and play an important role in biology and pharmacy, and as laboratory reagents [4].

Glutamine is the most abundant amino acid in the bloodstream, primarily contributing to wound healing [5–8], protection against inflammatory bowel disease [9–13], reducing weight also in HIV/AIDS patients [14, 15], and used in therapeutic treatment [16] for cancer patients [17–21] and also for obesity [22]. Glutamine, usually in the form of L-glutamine, is available as an individual supplement or as part of a protein supplement. Glutamine is one of the most abundant amino acids and participates in a variety of physiological functions, namely as a major fuel source for enterocytes, as a substrate for neoglucogenesis in kidney, lymphocytes, and monocytes, and as a nutrient/substrate in muscle protein metabolism in response to infection, inflammation, and muscle trauma [23]. Glutamine may help protect against some of the side effects of cancer chemotherapy and radiotherapy. Glutamine Schiff base copper complexes have potential use in cancer treatment and prevention [24].

Over the past 2 to 3 decades, gallium compounds have gained importance in the fields of medicine and electronics. In clinical medicine, radioactive gallium and stable gallium nitrate are used as diagnostic and therapeutic agents in cancer and disorders of calcium and bone metabolism. Some workers [25] studied the medical applications and toxicities of gallium compounds. Gallium compounds, whether used medically or in the electronics field, have toxicities. They are involved in problems related to

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environmental pollution (Ga compounds are used in the electronics industry) and to clinical treatments (Ga radionuclides are employed to detect neoplastic lesions). Moreover, since its chemical behavior is similar to that of aluminum, gallium could play a role in the health effects attributed to this element. Biologically, gallium is able to interrupt iron metabolism. Exposure to gallium has been shown to affect the human immune system [26]. The trivalent gallium cation is capable of inhibiting tumor growth, mainly because of its resemblance to the ferric ion [27]. Gallium(III) complexes acting as potent proteasome inhibitors [28] have a great potential to be developed into novel anticancer drugs. Gallium complexes can inhibit the tumor cellular proteasome and induce apoptosis [29].

Recently, interest in the use of metallic compounds for cancer treatment has been increasing since the discovery of cisplatin as an anticancer drug [26]. Clinical studies suggest the use of proteasome inhibitors as potential novel anticancer agents, and gallium toxicity can be reduced by complex formation.

The reduction of Ga(III) at the dropping mercury electrode (DME) in various complexing and non-complexing media [30–41] has been found. Voltametric [42–45], potentiometric [46–50], and spectrophotometric [51–65] studies on the complexes of gallium(III) have been reported. In this paper, electrochemical studies on the Ga(III)-glutamine system were carried out in order to investigate the formation of the complexes in aqueous solution. Several electrochemical methods have been employed to determine the stability constants of equilibria involving a metallic ion and ligands, but one of the most widely used is based on polarographic determinations when irreversibility conditions are attained. Our earlier investigations [66–70] on the complexation process in aqueous-nonaqueous mixtures furnished significant polarographic data pertaining to the stability and composition of the complex species. In sequence to these studies, the gallium-glutamine system was further investigated using aqueous media.

Results and discussion

Reduction

Ga(III) in L-glutamine ([Ga(III)] = 0.001 M, $\mu = 0.1$ M KNO_3) was initially investigated at pH 3.5 at 30 °C. The metal ion was observed to give a well-defined, diffusion-controlled wave in all solutions. The conventional log plots were linear, but the resulting slopes were not found to be in agreement with the theoretical values, thus indicating the irreversible nature of the electrode reaction.

Effect of concentration of the ligand

It is seen from Fig. 1 that the gallium-L-glutamine reduction wave, however, remained irreversible, and diffusion was controlled in all concentrations of the ligand (0.01–0.03 M) corresponding to 0.001 M Ga(III) in the presence of 0.1 M KNO_3 as supporting and 0.002% Triton-x-100 as maximum suppressor at pH 3.5. The wave nature did not change at higher temperatures of 40 °C as well. The number of electrons (n) involved in the electro-reduction was determined by the millicoulometric method [71] and was found to be 3 for Ga(III). Knowing the value of n, the diffusion coefficient ($D^{1/2}$) of the depolarizer was calculated by the Ilkovic equation (1) at different concentrations of L-glutamine.

$$i_d = 607nCD^{1/2}m^{2/3}t^{1/6} \quad (1)$$

The current at the end of the drop life was recorded instead of the average current, because the determination of kinetic parameters is based on Koutecky's method [72], which is more accurately reproduced by measuring the maximum current [74]. The various criteria [74–77] of irreversibility indicate that the electrode reaction of Ga(III) is irreversible.

The plots of i_d versus $h_{eff}^{1/2}$ were found to be linear and passing through the origin, thereby indicating the diffusion-controlled nature of the reduction.

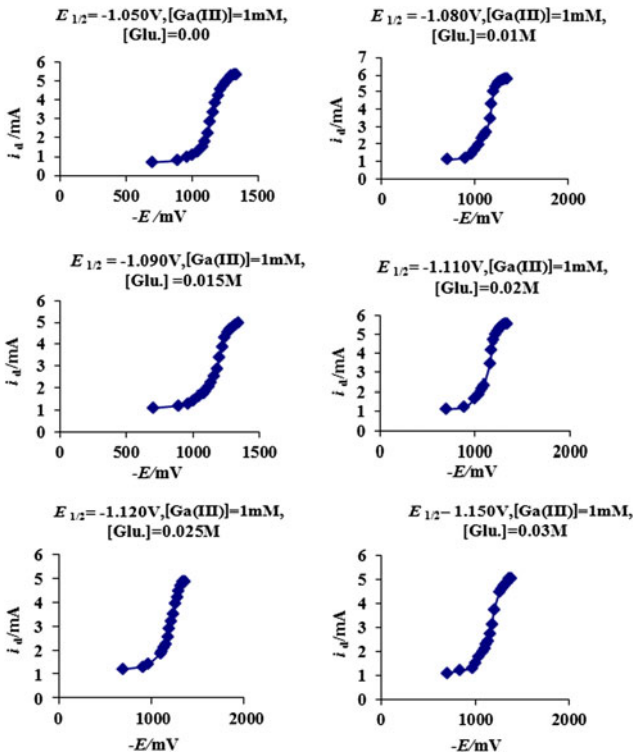

Fig. 1 Polarograms of the [Ga(III)]-glutamine system at 30 °C

Kinetic parameters

Koutecky's treatment [72] of irreversible waves as extended by Meites and Israel [73] was applied for determining the kinetic parameters, viz. transfer coefficient (α_n) and formal rate constant ($k^0_{f,h}$), for the electrode reaction by using Eqs. (2) and (3):

$$E_{d.e.} = E_{1/2}\frac{0.0542}{\alpha_n}\log\frac{i_d}{i_d - i} \quad (2)$$

where

$$E_{1/2} = -0.2412 + \frac{0.05915}{\alpha_n}\log\frac{1.349k^\circ_{f,h}t^{1/2}}{D^{1/2}} \quad (3)$$

The kinetic parameters have been thus calculated by employing Eqs. (2) and (3).The value of α_n was determined by equating the slope of plots $-E_{1/2}$ versus log i/i_{d-i} to $0.0542/\alpha_n$, and the intercept ($E_{1/2}$) was used to calculate $k^0_{f,h}$ at different concentrations of ligand, after getting the values of $D^{1/2}$ from the Ilkovic equation. The effect of increasing concentration of ligand (0.01–0.03) on polarographic characteristics, viz. i_d, $E_{1/2}$ and $D^{1/2}$, and kinetic parameters at 30 °C and 40 °C are summarized in Table 1.

From the perusal of the result, $E_{1/2}$ values shifted to more negative potentials revealing complex formation. A perusal of the values of α_n reveals that α_n decreases with increasing concentration of L-glutamine, which implies [78] that the transfer of electrons is made increasingly difficult. In other words, the electrode reaction of Ga(III) is rendered increasingly irreversible with an increase in L-glutamine concentration. Decreasing value of $k^0_{f,h}$ also indicate [79] the increased irreversibility of the electrode reaction of Ga(III) with increasing concentrations of L-glutamine.

The reduction of Ga(III) in L-glutamine was found irreversible. The values of the overall formation constant B_j were calculated by the graphical extrapolation method [80].The experimentally determined values calculated for Ga(III)-L-glutamine are recorded at 303 and 313 K. The overall formation constants were obtained by extrapolation of $F_j[(X)]$ functions to the zero ligand concentration. The values of stability constants of Ga(III)-L-glutamine at 303 K are $\beta_1 = 1.35$, $\beta_2 = 6.5$, and $\beta_3 = 1{,}350$, and at 313 K are $\beta_1 = 0.95$, $\beta_2 = 5$, and $\beta_3 = 1{,}220$.

Thermodynamic functions

The enthalpy of activation ($\Delta H°$) for the electrode reaction has been calculated by equating the slope of plot log $k^0_{f,h}$ versus $1/T$ to $-\Delta H°/2.303R$ and found to be 24.87 kJ/mol at 30 °C.

The free energy of activation ($\Delta G°$) could be determined from Eq. (4).

$$k^\circ_{f,h} = \frac{kT}{h}\varphi\exp\left[\frac{\Delta G^\circ}{RT}\right] \quad (4)$$

where k = Boltzmann's constant, h = Planck's constant, and $\varphi = 2.0 \times 10^{-8}$ cm. The value of $\Delta G°$ at 30 °C was found to be 23.86 kJ/mol.

Table 1 Polarographic data for Ga(III)-L-glutamine ([Ga(III)] = 0.001 M, α = 0.1 M KCl, pH 3.5)

Conc. of ligand (M)	Intercept $-E_{1/2}$ (V)	$D^{1/2}$ [(cm/s)$^{1/2}$]	i_d (μA)	α_n	Log $k^0_{f,h}$	$k^0_{f,h}$ (cm/s)
0.000						
(a)	1.050		5.15	0.264		
(b)	1.00		5.2	0.271		
0.01						
(a)	1.080	0.097	4.8	0.190	−4.06	8.70×10^{-5}
(b)	1.020	0.103	5.05	0.195	−3.91	1.23×10^{-4}
0.015						
(a)	1.090	0.058	4.3	0.168	−4.00	1.00×10^{-4}
(b)	1.0388	0.065	4.85	0.170	−3.83	1.47×10^{-4}
0.02						
(a)	1.110	0.043	4.3	0.144	−3.84	1.44×10^{-4}
(b)	1.0465	0.043	4.25	0.150	−3.76	1.73×10^{-4}
0.025						
(a)	1.120	0.032	3.95	0.120	−3.67	2.13×10^{-4}
(b)	1.0640	0.033	4.15	0.135	−3.71	1.94×10^{-4}
0.03						
(a)	1.150	0.026	3.9	0.110	−3.63	2.34×10^{-4}
(b)	1.800	0.027	4.0	0.125	−3.70	1.99×10^{-4}

(a) At 30 °C; (b) at 40 °C

The entropy of activation of ($\Delta S°$) at 30 °C calculated from Eq. (5) was found to be 3.31 J/mol K.

$$\Delta S^\circ = \frac{\Delta H^\circ - \Delta G^\circ}{T} \quad (5)$$

Conclusions

In this article, the interaction of Ga(III) and L-glutamine at pH 3.5 was investigated using a polarographic method. The results indicated that current voltage curves were irreversible and diffusion controlled in 0.1 M KNO_3 at pH 3.5 at 30 and 40 °C. The values of kinetic parameters, transfer coefficient (α_n), and formal rate constant ($k^0_{f,h}$) of the electrode reactions have been calculated by Koutecky's method. The positive free energy change ($\Delta G°$) indicates that the reduction is endergonic, the positive values of $\Delta H°$ indicated the endothermic nature of the metal-ligand interaction, and the change in entropy ($\Delta S°$) value indicates that the system has become more disordered.

Experimental

Reagents

All chemicals used were of analytical grade, and the stock solutions were prepared in double-distilled water. Potassium nitrate (0.1 M) was used as the supporting electrolyte and Triton-x-100 (0.002%) as maximum suppressor. The concentration of metal ion in test solutions was 1.0 mM. The pH of the test solution was adjusted to 3.5 using dilute HCl or NaOH solutions. The concentration of the ligand was varied from 0.01 to 0.03 mol/dm^3.

Apparatus

An Elico digital polarograph (CL-357) was used for obtaining the current voltage curves. The polarograph contained a counter electrode, slandered calomel electrode, and DME. Deoxygenation of solutions was done by bubbling purified nitrogen for 15 min. The potentials were measured against a saturated calomel electrode (SCE). An $U7^c$-type German thermostat having an accuracy of ±0.1 °C was employed to maintain a constant temperature throughout all the experiment work. The pH measurements were carried out by a Toshnial CL 54 pH meter (accuracy ±0.01 pH). The instrument was calibrated using slandered buffers of different pH values before and after each series of measurements. The capillary had the following characteristics: $m = 4.66$ mg/s, $t = 3.0$ s, and $m^{2/3}t^{1/6} = 3.350$ at $h_{Hg} = 100$ cm.

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