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Quantification of Cr(VI)-Thymoquinone Complex Using Cyclic Voltammetry

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Abstract. Quantitative studies of Cr(VI)- thymoquinone complex have been performed by cyclic voltammetry. For this purpose glassy carbon, platinum and saturated calomel electrodes were used as working, auxiliary and reference electrodes, respectively. The effects of concentrations and metal-ligand ratios on Cr(VI)-thymoquinone complex were investigated. Effect of concentration was found to follow Randles-Sevcik equation. Calibration curve method with linear regression line confirms that cyclic voltammetry can be used for quantification of Cr(VI)-thymoquinone complex for pharmaceutical assay. Complete complex formation seems to occur at metal ligand ratio 1:1. Results indicate quasi-reversible electron transfer mechanism. E° and diffusion coefficient of complex at different concentrations and metal ligand ratios were also calculated and found to be 0.244±0.01 V and 3.45×10^{-5} cm^2s^{-1}, respectively. The values of transfer coefficients, α and β, were found to be 0.716±0.02-1.231±0.01 and 0.814±0.01-0.906±0.01, respectively.

Keywords: Cr(VI)-thymoquinone complex, quantitative studies, cyclic voltammetry

Introduction

Electrochemical methods are now emerging as powerful and versatile analytical techniques and have found vast applications in many important fields including pharmaceutical industry, and biological and environmental applications (Farghaly *et al*., 2014; Tsai *et al*., 2011; Sivasubramanian and Sangaranarayanan, 2011; Beitollahi *et al*., 2008). The use of electro analysis is increasing day by day due to high sensitivity, reduction in solvent and sample consumption, high-speed and low operating cost (Almeida *et al*., 2013; Halls *et al*., 2013; Yuzhi Li *et al*., 2013; Cheng *et al*., 2012; Aaboubi and Housni, 2012; Farghaly *et al*., 2005; Farghaly and Ghandour, 2005). Especially voltammetric techniques have proved to be more suitable to investigate the redox properties of drugs and biological analytes (Baghbamidi *et al*., 2012; Karaaslan and Suzen, 2011).

Cyclic voltammetry is a potentiodynamic electrochemical technique. The primary function of this technique is to give qualitative information regarding various electrochemical processes, although it is equally beneficial for quantitative analysis. It is useful in finding out the mechanisms and kinetics of different electrochemical reactions, rates of oxidation/reduction processes, stability of different oxidation states etc. Furthermore, this technique helps to give information about the presence of intermediates in various redox reactions (Skoog *et al*., 1998; Braun, 1983). Hence, this technique is very popular and reliable electrochemical technique and widely used nowadays (Beitollahi and Mostafavi, 2014; Molaakbari *et al*., 2014; Baghbamidi *et al*., 2012; Beitollahi and Sheikhshoaie, 2011; Beitollahi *et al*., 2012).

Thymoquinone (2-methyl-5-isopropyl-1,4-benzoquinone) is a phytochemical compound (Fig. 1). It is found as an active component in the plant of *Nigella sativa* (Ali and Blunden, 2003). It possesses several biological activities (Gali-Muhtasib *et al*., 2008; Syed, 2008; Badary *et al*., 2007; El-Mahdy *et al*., 2005). Most of its pharmacological properties are due to its antioxidant property (Mansour *et al*., 2002). In addition, it has the ability to form complexes. Previously its complexation with some redox active metals using potentiometry has been investigated by Kishwar *et al*. (2012). The complexation of thymoquinone with iron by cyclic voltammetry has also been examined qualitatively and quantitatively by Kishwar and Haq (2013).

Chromium (VI) has been reported as a highly toxic element. It is a strong irritant; as a result it may cause different types of allergic reactions. Its inhalation can

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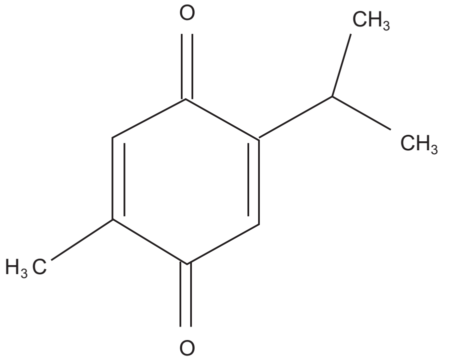

Fig. 1. Structure of thymoquinone.

cause irritation and damage to nose, lungs, stomach and intestine and ingestion could result in stomach malfunctioning and ulcers, convulsions, damage to kidney and liver and even death. In case of chronic exposure it might cause pulmonary fibrosis and lung cancer. However, certain reducing substances in the food could reduce Cr(VI) to Cr(III) (Stoecker, 1999; Lukaski, 1999). Seeds of *Nigella sativa* are commonly used in our food and thymoquinone in these seeds can also perform the same function. Cr(VI) forms a vast variety of complexes (Sharpe, 1996) including complex with thymoquinone (Kishwar *et al*., 2012). Hence, it could be helpful in case of Cr(VI) toxicity. In this view quantitative study of Cr(VI)-thymoquinone complex was performed in order to get useful information regarding complexation of Cr(VI) and thymoquinone.

Materials and Methods

Instrumentation. ***Cyclic voltammeter.*** CHI–760 D Electrochemical work station was used. Three electrodes were used, a glassy carbon working electrode (Model number = CHI 104, area of the electrode = 0.07065 cm^2), saturated calomel reference electrode and a platinum wire auxiliary electrode. The working electrode was repolished using alumina, the particles' size of which was 0.3 micron.

Chemicals. Thymoquinone was purchased from MP Biomedicals, LLC, whereas sodium chloride and potassium dichromate from E. Merck.

Sample preparation. ***Supporting electrolyte.*** 0.1 M solution of NaCl.

Analyte solution. The 5×10^{-3} M solution of thymoquinone (TQ) and equimolar solution of $K_2Cr_2O_7$ were prepared as measuring solution. TQ was analyte. 10% methanol was also used in their preparation in addition to 0.1 M NaCl.

Cyclic voltammetric studies. At first CV of supporting electrolyte was run to get base-line and then 15.0 mL of 5×10^{-3} M solution of analyte and equimolar solution of metal were run to get overlay. The scan rate and current sensitivity were 0.1 V/s and 1×10^{-4} A/V, respectively. The potential range was set from -0.40 V to +0.80 V and then reversed back to -0.40 V. In order to observe effect of several parameters, the complexation was studied by varying metal ligand ratio and concentration.

Complex solutions having different metal-ligand ratio from 1:0.5 to 1:5 and concentrations from 0.02×10^{-3} M to 1.2×10^{-3} M were prepared in order to investigate effect of these changes on complex formation.

Results and Discussion

Effect of concentration on voltammograms of Cr(VI)-thymoquinone complex. Calibration curve method was used to judge effect of concentration on Cr(VI)-thymoquinone complex. For this Randles-Sevcik equation (Greef *et al*., 1985) was used which is as follows:

$$I_p = 0.4463\ nFACo^*\ (nF\ \nu\ D^\circ/RT)^{1/2}$$

where:

I_p = peak current (A); ν = scan rate (V/s); n = number of electron transferred; F = Faraday's constant; A = area of electrode (cm^2); Co* = concentration of Cr(VI)-thymoquinone complex (moles/cm^3); D° = diffusion coefficient of Cr(VI)-thymoquinone complex ($cm^2\ s^{-1}$); T = 25 ± 2 °C and R = rate constant.

The cyclic voltammograms at different concentration showed dependence of I_p on concentration of the complex. At low concentrations, 0.02×10^{-3} M and 0.1×10^{-3} M, no oxidative wave of forward scan was observed whereas the reduction peak could be seen clearly during the reverse scan. It was observed that one small peak (1) is also appearing in addition to a bigger peak (3) in both forward as well as in reverse scan (Fig. 2a). It may be due to complications in the reaction. It is possible that the metal needs low concentration of the ligand for complex formation and excess ligand may be responsible for giving bigger peaks, as these peaks (i.e., peak 3 and 4) were observed within the potential range similar to that of thymoquinone (Table 1-2). Direct increase of current with concentration (0.02×10^{-3} M to 1.2×10^{-3} M) shows that effect of concentration follows Randles - Sevcik equation (Fig. 2b). Calibration curve along with least square fit line showed no major deviation from zero, which points out towards the possibility that no adsorption has occurred on electrode surface. These results indicate that calibration curve method can be used for quantification of Cr(VI)-thymoquinone complex within a wide range i.e. (0.2×10^{-3} M to 1.2×10^{-3} M).

Effect of metal-ligand ratio. For this purpose cyclic voltammograms of complex solutions having metal-ligand ratios 1:0.5 -1:5 were studied. The overlay reveals

Table 1. Electrochemical parameters of cyclic voltammograms of thymoquinone, Cr(VI), and Cr(VI)-thymoquinone complex

	I_{pa} ($\times10^{-5}$ A)	I_{pc} ($\times10^{-5}$ A)	E_{pa} (V)	E_{pc} (V)
TQ	1.017 ±0.01	2.717 ±0.01	-0.242 ±0.01	-0.326 ±0.01
Cr(VI)	-	-	-	-
Cr(VI)-TQ complex	0.246 ±0.01	1.142 ±0.01	0.179 ±0.01	-0.210 ±0.01

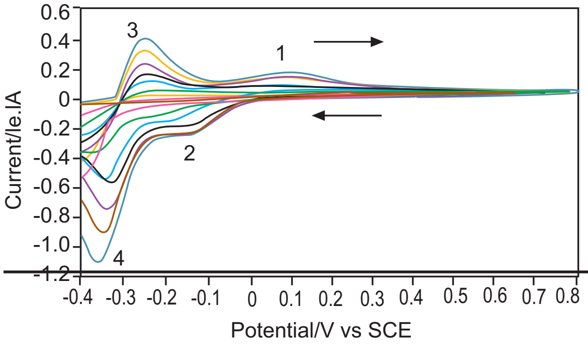

Fig. 2a. Cyclic- voltammograms of Cr(VI)-thymoquinone complex showing effect of concentration (concentrations of complex solutions = 0.02×10^{-3} M, 0.1×10^{-3} M, 0.2×10^{-3} M, 0.4×10^{-3} M, 0.6×10^{-3} M, 0.8×10^{-3} M, 1×10^{-3} M, 1.2×10^{-3} M).

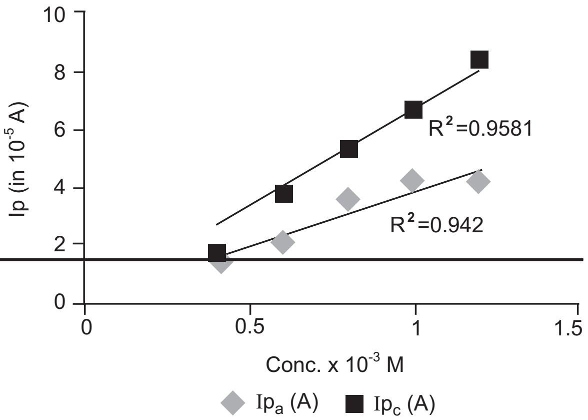

Fig. 2b. Plot of anodic and cathodic peak current against concentration of Cr(VI)-thymoquinone complex.

Table 2. The values of E_p, $E_{p/2}$, E_p-$E_{p/2}$, E_{pa}-E_{pc},, I_p, αn_a, βnb and diffusion coefficients from cyclic voltammograms of Cr(VI)-thymoquinone complex with different concentrations

Concentration (10^{-3} M)	E_{pa} (V)	$E_{pa/2}$ (V)	E_{pa}-$E_{pa/2}$ (V)	I_{pa} $\times10^{-5}$(A)	I_{pa}/I_{pc}	βn_b $=0.048/E_{pa}$-$E_{pa/2}$	D (cm² s⁻¹)
0.02	-0.236 ± 0.01	-0.29 ± 0.01	0.054 ± 0.011	1.431 ± 0.01	1.15	0.889 ± 0.01	-
0.4	-0.238 ± 0.01	-0.292 ± 0.01	0.054 ± 0.011	1.507 ± 0.01	0.88	0.889 ± 0.01	1.90×10^{-5}
0.6	-0.24 ± 0.01	-0.294 ± 0.01	0.054 ± 0.011	2.143 ± 0.01	0.566	0.889 ± 0.01	1.7×10^{-5}
0.8	-0.247 ± 0.02	-0.3 ± 0.02	0.053 ± 0.012	3.419 ± 0.02	0.65	0.906 ± 0.02	2.44×10^{-5}
1.0	-0.248 ± 0.02	-0.301 ± 0.02	0.053 ± 0.011	4.099 ± 0.02	0.61	0.906 ± 0.01	2.24×10^{-5}
1.2	-0.248 ± 0.02	-0.301 ± 0.02	0.053± 0.012	4.252 ± 0.02	0.508	0.906 ± 0.02	1.68×10^{-5}

Concentration (10^{-3} M)	E_{pc} (V)	$E_{pc/2}$ (V)	E_{pc}-$E_{pc/2}$ (V)	E_{pa}-E_{pc} (V)	I_{pc} $\times10^{-5}$(A)	αn_a $=0.048/E_{pc}$-$E_{pc/2}$	D (cm² s⁻¹)
0.02	-0.377 ± 0.02	-0.333 ± 0.02	-0.041 ± 0.011	0.141 ± 0.01	1.248 ± 0.02	1.2 ± 0.02	-
0.4	-0.375 ± 0.01	-0.33 ± 0.01	-0.045 ± 0.012	0.137 ± 0.01	1.706 ± 0.01	1.1 ± 0.01	2.43×10^{-5}
0.6	-0.353 ± 0.01	-0.312 ± 0.01	-0.041 ± 0.011	0.113 ± 0.01	3.785 ± 0.01	1.20 ± 0.01	5.31×10^{-5}
0.8	-0.348 ± 0.01	-0.295 ± 0.01	-0.053 ± 0.011	0.101 ± 0.01	5.248 ± 0.01	0.906 ± 0.01	5.75×10^{-5}
1.0	-0.342 ± 0.02	-0.294 ± 0.02	-0.048 ± 0.012	0.094 ± 0.01	6.716 ± 0.02	1.0 ± 0.01	6.02×10^{-5}
1.2	-0.35 ± 0.01	-0.301 ± 0.01	-0.049 ± 0.012	0.102 ± 0.01	8.37 ± 0.01	0.980 ± 0.01	6.50×10^{-5}

that complete complexation occurred at metal ligand ratio 1:1 because here anodic and cathodic peaks (1 and 2) were observed in a potential range entirely different from that of thymoquinone (Table 3, Fig. 3). By further increasing metal-ligand ratio, sudden change in the peak potential was observed. These observations suggest that probably thymoquinone suppressed the metal at high concentrations and its own peaks (3 and 4) became prominent. At higher metal-ligand ratios i.e., 1:3-1:5 distortion in the anodic peaks was observed which may be due to the superimposition of two peaks lying very close to each other. These two peaks may be of complex and thymoquinone.

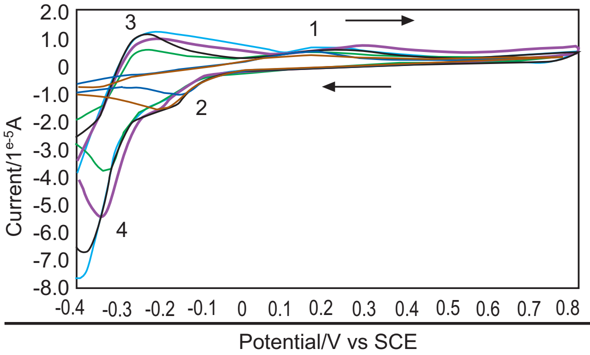

Fig. 3. Cyclic- voltammograms of Cr(VI)-thymoquinone complex showing effect of metal - ligand ratio (Metal-ligand Ratio = 1:0.5, 1:1,1:2,1:3, 1:4, 1:5, concentration of TQ = 5×10^{-3} M, concentration of Cr(VI) solution = 5×10^{-3} M).

In case of effect of metal-ligand ratio the cyclic voltammograms seem to fulfill the criteria for quasi-reversible reactions (Bard and Faulkner, 2001). As I_{pa}/I_{pc} was not equal to one and ΔE_p was found to be greater than 59/n mV, it seems that quasi-reversible behaviour is favoured (Table 3). For each case α and β were also calculated using the relation 0.048/E_p-$E_{p/2}$ which were found in the range of 0.716 ± 0.02 to 1.231 ± 0.01 and 0.814 ± 0.01to 0.906 ± 0.01, respectively. Effect of metal-ligand ratio on peak potential (E_{pa} and E_{pc}) gave a straight line with very good R^2 value (Fig. 4), showing independence of peak potential on change in metal ligand ratio.

An increase in I_{pa} and I_{pc} was noted with the increase in metal-ligand ratio but the peak current became nearly constant at metal-ligand ratio 1:3, showing nearly maximum complexation below this ratio (Fig. 5).

Analysis of diffusion coefficient for Cr(VI)-thymoquinone complex. Diffusion coefficient of different complexes and compounds is an important constant and it could be easily and accurately measured by cyclic

Table 3. The values of E_p, $E_{p/2}$, E_{pa}-E_{pc}, I_p and αn_a, βn_b and diffusion coefficients from cyclic voltammograms of Cr(VI)-thymoquinone complex with different metal-ligand ratios

Ratio L/M	E_{pa} (V)	$E_{pa/2}$ (V)	E_{pa}-$E_{pa/2}$ (V)	I_{pa} ×10^{-5}(A)	I_{pa}/I_{pc}	βn_b =0.048/E_{pa}-$E_{pa/2}$	D ($cm^2\ s^{-1}$)
0.5	0.149 ± 0.01	0.09 ± 0.01	0.059 ± 0.01	0.2 ± 0.01	0.256 ± 0.01	0.814 ± 0.01	-
1	0.179 ± 0.01	0.12 ± 0.01	0.059 ± 0.01	0.246 ± 0.01	0.215 ± 0.01	0.814 ± 0.01	-
2	-0.232 ± 0.01	-0.29 ± 0.01	0.058 ± 0.01	0.932 ± 0.01	0.46 ± 0.01	0.828 ± 0.01	4.64 × 10^{-6}
3	-0.236 ± 0.02	-0.291 ± 0.01	0.055 ± 0.02	1.431 ± 0.01	0.434 ± 0.01	0.873 ± 0.02	1.09 × 10^{-5}
4	-0.239 ± 0.01	-0.292 ± 0.01	0.053 ± 0.01	1.411 ± 0.01	0.352 ± 0.01	0.906 ± 0.01	1.06 × 10^{-5}
5	a	-	-	-	-	-	

Ratio L/M	E_{pc} (V)	$E_{pc/2}$ (V)	E_{pc}-$E_{pc/2}$ (V)	E_{pa} - E_{pc} (V)	I_{pc} ×10^{-5}(A)	αn_a =0.048/E_{pc}-$E_{pc/2}$	D ($cm^2\ s^{-1}$)
0.5	-0.17 ± 0.01	-0.103 ± 0.02	-0.067 ± 0.02	0.021 ± 0.02	0.78 ± 0.01	0.716 ± 0.02	-
1	-0.21 ± 0.01	-0.15 ± 0.01	-0.06 ± 0.01	0.031 ± 0.02	1.142 ± 0.01	0.8 ± 0.01	-
2	-0.338 ± 0.01	-0.299 ± 0.01	-0.039 ± 0.01	0.106 ± 0.01	2.028 ± 0.01	1.231 ± 0.01	2.2 × 10^{-5}
3	-0.346 ± 0.01	-0.302 ± 0.01	-0.044 ± 0.01	0.11 ± 0.01	3.3 ± 0.01	1.091 ± 0.01	5.82 × 10^{-5}
4	-0.37 ± 0.01	-0.31 ± 0.01	-0.06 ± 0.02	0.131 ± 0.02	4.011 ± 0.01	0.8 ± 0.01	8.59 × 10^{-5}
5	-	-	-	-	-	-	

a = peak distorted.

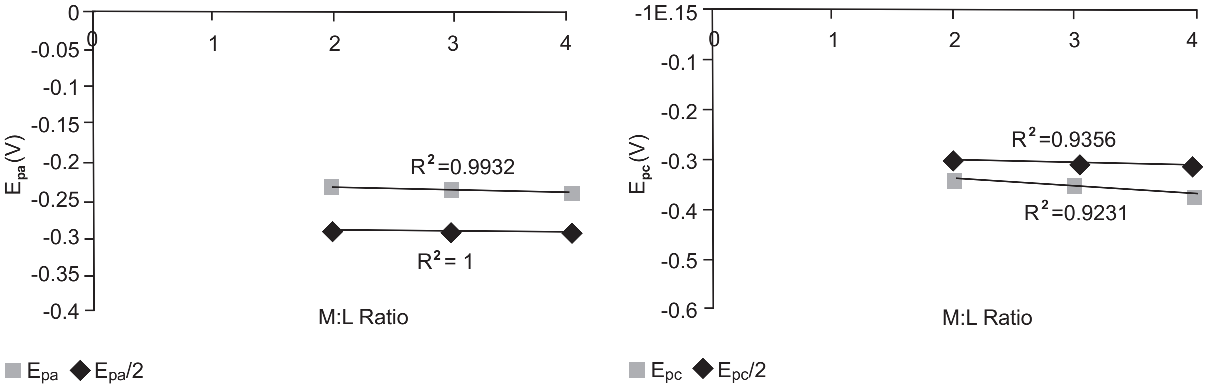

Fig. 4. Variation of anodic and cathodic peak potentials with change of metal-ligand ratio in cyclic voltammograms of Cr(VI)-thymoquinone complex.

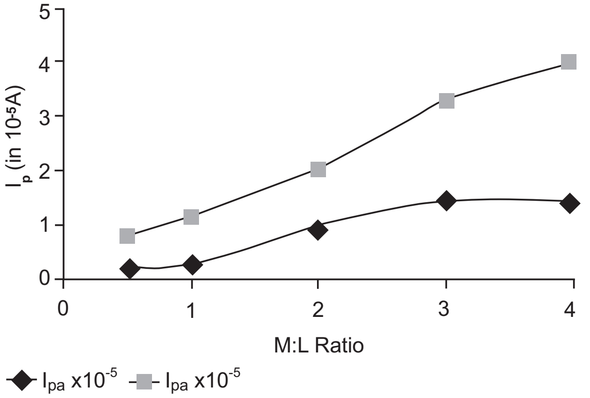

Fig. 5. Variation of anodic and cathodic peak currents with change of metal-ligand ratio in cyclic voltammograms of Cr(VI)-thymoquinone complex.

voltammetry (Anwer, 2006). Diffusion coefficient of the complex was determined using Randles- Sevcik (Greef *et al.*, 1985) equation by varying concentrations and metal-ligand ratios (Table 2-3). No reasonable effect of varying concentration or metal-ligand ratio on diffusion coefficient was observed and its value remained nearly the same under all above mentioned conditions. Area of electrode (A) was 0.07065 cm^2 whereas number of electron transfer (n) was supposed to be 3 (Sharpe, 1996).

Analysis of E°, a characteristic property. For Cr(VI)-thymoquinone complex values of E° were determined at different concentrations and metal-ligand ratios and it was found to be approximately constant at all concentration and ratios (Table 4), except in first two cases of metal- ligand ratio. This change may be due to the fact that in case of metal- ligand ratio 1:0.5 and 1:1anodic and cathodic peaks (1 and 2 in Fig. 3) were observed in a potential range entirely different than rest of the metal-ligand ratios. Hence, it is suggested that change in peak potential, both in E_{pa} and E_{pc} (Table 3), resulted in changed values of E°.

Table 4. Half wave potential (E°= $E_{1/2}$) for Cr(VI)-thymoquinone complex at different concentrations and metal-ligand ratios

Concentration (10^{-3} M)	$(E°)_a$ (V)	Ratio L/M	$(E°)_a$ (V)
0.02	0.264 ± 0.01	0.5	0.12 ± 0.02
0.4	0.265 ± 0.01	1	0.15 ± 0.02
0.6	0.267 ± 0.01	2	0.261 ± 0.02
0.8	0.274 ± 0.02	3	0.264 ± 0.01
1.0	0.275 ± 0.02	4	0.266 ± 0.01
1.2	0.275 ± 0.02	5	-

Briefly, quantitative studies of Cr(VI)-thymoquinone complex were performed at glassy carbon electrode against saturated calomel electrode which include determination of E°, D, α, and β. Effects of different parameters, i.e., concentration and metal ligand ratio, on complexation were observed by varying these parameters. Horizontal base line indicates the purity of the base electrolyte. The Cr(VI)-thymoquinone complex seems to be stable at lower concentrations. It was also suggested that here best complex formation occurred at metal-ligand ratio 1:1. At higher metal- ligand ratios (i.e., 1:2 to 1:5) distortion in the anodic peak was observed which may be due to the presence of two peaks very close to each other. Present study reveals that calibration curve method by cyclic voltammetry can be helpful in quantification of Cr(VI)-thymoquinone complex. E° was observed to be approximately constant. Diffusion coefficient was calculated using Randles- Sevick equation. The values of transfer coefficients, α, and β were also determined at different concentrations and metal-ligand ratios.

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