Chinese Journal of Chemistry, **2006**, *24*, 1657—1661 **Note**

Catalytic Adsorptive Stripping Voltammetry at a Carbon Paste Electrode for the Determination of Amiodarone

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Voltammetry using solid electrodes usually suffers from the contamination due to the deposition of the redox products of analytes on the electrode surface. The contamination has resulted in poor reproducibility and overelaborate operation procedures. The use of the chemical catalysis of oxidant on the reduction product of analyte not only can eliminate the contamination of analyte to solid electrodes but also can improve the faradaic response of analyte. This work introduced both the catalysis of oxidant $K_2S_2O_8$ and the enhancement of surfactant Triton X-100 on the faraday response of amiodarone into an adsorptive stripping voltammetry at a carbon paste electrode for the determination of amiodarone. The method exhibits high sensitivity, good reproducibility and simple operation procedure. In 0.2 mol•L^{-1} HOAc-NaOAc buffer (pH＝5.3) containing 2.2×10^{-2} mol•L^{-1} $K_2S_2O_8$ and 0.002% Triton X-100, the 2.5th-order derivative stripping peak current of the catalytic wave at 0.3 V (vs. Ag/AgCl) is rectilinear to amiodarone concentration in the range of 2.0×10^{-10}—2.3×10^{-8} mol•L^{-1} with a detection limit of 1.5×10^{-10} mol•L^{-1} after accumulation at 0 V for 30 s.

Keywords amiodarone, Triton X-100, peroxysulfate, catalytic adsorptive stripping voltammetry, carbon paste electrode

Introduction

Amiodarone hydrochloride, an antianginal and antiarrhythmic drug, is used for the treatment of various supraventricular and ventricular arrhythmias. Except high-performance liquid chromatography,[1-4] fluorescent spectroscopy[5] and capillary electrophoresis,[6] electrochemical methods for the determination of amiodarone, including potentiometry,[7] polarography[8] and voltammetry,[9] have been reported. Tan and coworkers[8] reported a single sweep polarographic method for the determination of amiodarone in 0.2 mol•L^{-1} $NaHPO_4$-KH_2PO_4 (pH 6.8) buffer. The detection limit was about 5.0×10^{-8} mol•L^{-1}. The toxicity of mercury limited the applications of the polarographic method. Hermosa and coworkers[9] reported a voltammetric method based on electro-oxidation of amiodarone at a carbon paste electrode (CPE) in phosphate buffer-acetonitrile media, with detection limit of 4.0×10^{-6} mol•L^{-1}. In the voltammetric method using solid electrodes, not only the lack of sensitivity, but also the deposition contamination of redox products of analytes at solid electrodes has yet led to the reduction of analytical performance, such as the poor reproducibility, the overelaborate operation procedures and others.

It is known that the catalytic technique, based on a redox cycle that the electrochemical reduction of analyte occurs simultaneously with the chemical oxidation of its reduction product by oxidant, has been used in polarography,[10-13] and has improved the sensitivity of polarographic determination of organic compounds by 1—2 orders in magnitude.[14-16] Perceptibly, introducing it to voltammetric determination not only could improve the sensitivity but also could eliminate the contamination from reduction product of analyte to solid electrodes. However, no work has been reported in literature for the determination of organic compounds by the catalytic voltammetry using solid electrodes. In addition, the poor solubility of many organic compounds in low molecular weight aggregate forms in aqueous solution would often result in low sensitivity. The surfactant aggregates formed in aqueous solution could improve the solubility of analyte in water, and surfactants could improve the accumulation characteristics of analyte on the electrode surface as well. With these actions of surfactants, the sensitivity and the selectivity of polarographic and voltammetric methods for the determination of metal ion complexes and organic substances have been modified.[17-21]

In this work, therefore, both the catalytic action caused by oxidant $K_2S_2O_8$ and the enhancement action of surfactant Triton X-100 on faraday response of amiodarone were incorporated with adsorptive stripping voltammetry, developing a catalytic adsorptive stripping voltammetric method (CAdSV) for the determination of amiodarone at the CPE. The proposed method shows good reproducibility, high sensitivity and simple operation procedure.

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Experimental

Reagents

1.0×10^{-3} mol•L^{-1} Stock standard solution of amiodarone hydrochloride (Shanghai Jiufu Pharmaceutical Co. Shanghai, China) was prepared to be an ethanol-water (50∶50, *V*∶*V*) solution. The solution was kept in a brown volumetric flask. Standard working solutions were prepared by appropriately diluting the stock standard solution with water. A series of HOAc-NaOAc buffers (pH 3.5—6.2), Triton X-100 (w=0.01%, Chemically pure, Beijing Chemical Reagent Factory, Beijing, China) solution and 0.1 mol•L^{-1} $K_2S_2O_8$ (Chemically pure, Yixing Chemical Reagent Factory No. 3, Yixing, China) solution were routinely prepared. Carbon powder (Beijing Chemical Reagent Factory, Beijing, China) was of spectral grade, and silicon oil (Kelong Chemical Reagent Factory, Chengdu, China) was of chromatographic grade. All other chemicals used were of analytical reagent grade. Twice distilled water was used throughout.

Apparatus

2.5th-order derivative single sweep voltammograms were recorded by a model JP3-1 polarographic analyzer (Shandong Electric & Telecommunication Factory No. 7, Jining, China). A three-electrode set-up was equipped with a home-made CPE working electrode, an Ag/AgCl reference electrode and a platinum-wire counter electrode. The potential scan rate was 0.3 V•s^{-1}. Unless otherwise stated, all potentials were referred to the potential of the Ag/AgCl electrode.

The CPE was prepared as described in the Ref. 12. In order to obtain a more sensitive and stable analytical signal, the CPE was first activated by cyclic potential scans between 1.0 and −0.5 V for 10 times in HOAc-NaOAc buffer (pH 5.3), and the stable background current was obtained.

Procedure

10 mL of 0.2 mol•L^{-1} HOAc-NaOAc buffer (pH 5.3) containing an appropriate amount of standard working solution or sample solution of amiodarone, 0.002% Triton X-100 and 0.02 mol•L^{-1} $K_2S_2O_8$ was transferred into a voltammetric cell. The potential of the CPE was controlled at 0 V and kept for 30 s for accumulation while the solution was stirred. After another 10 s, the 2.5th-order derivative single sweep voltammogram was recorded by applying a cathodic scan from 0.6 to 0.0 V at the rate of 0.3 V•s^{-1}. The 2.5th-order derivative peak current of the catalytic stripping wave of amiodarone at +0.3 V was measured. The calibration curve was obtained by plotting the 2.5th-order derivative peak current versus standard amiodarone concentration.

After each measurement, the CPE was rinsed in the HOAc-NaOAc buffer (pH 5.3) 3 times, and was directly used for the next measurement. If necessary, the surface was renewed by smoothing 2—3 mm of the carbon paste off, and was then polished and activated.

Analysis of pharmaceutical formulation

Ten tablets were weighed and powdered in a mortar. A weighed portion of the powder equivalent to one tablet was dissolved in 50 mL of 95% ethanol, transferred into 100 mL volumetric flask and diluted to the mark with water. The supernatant liquid was used to analysis. The measurement was performed according to the procedure mentioned above. The amiodarone content in tablets was determined by using the calibration curve.

Results and discussion

Voltammetric behavior of amiodarone

The voltammetric behavior of amiodarone was examined at the CPE in various supporting electrolytes. A single reduction wave appeared at 0.3 V in the HOAc-NaOAc buffer (pH 5.3), and the peak current of the reduction wave increased with the increase the amiodarone concentration, which indicated the reduction wave was confirmed to be the reduction of amiodarone. In view of its chemical structure, amiodarone was known as (2-butyl-3-benzofuranyl)[4-[2-(diethylamino)ethoxy]-3,5-diiodophenyl]methanone hydrochloride, and belongs to benzoyl derivatives. The polarographic behaviors of benzoyl derivatives such as fenofibrate, ketoprofen, amiodarone, mebendazole and flubendazole have been studied in aqueous and organic media and used for analytical purpose,[22-26] respectively. All these derivatives showed a polarographic reduction wave, which was attributed to the reduction of the electroactive benzoyl group via a two-electron and two-proton addition. From this, it can be deduced that the reduction wave of amiodarone at the CPE still is the reduction of the benzoyl group as well.

In the HOAc-NaOAc buffer (pH 5.3), $K_2S_2O_8$ itself did not display any voltammetric response in the potential range tested. However, when $K_2S_2O_8$ was added to the buffer containing amiodarone, the peak current of the reduction wave at 0.3 V increased dramatically, while the peak potential remained unchanged. These voltammetric characters indicated that the enhanced wave in the presence of $K_2S_2O_8$ was a parallel catalytic one.[13] It was considered that the parallel catalytic wave resulted from subsequent oxidation of the reduction product of the benzoyl group of amiodarone by both persulfate anion $S_2O_8^{2-}$ and sulfate radical anion $SO_4^{-\cdot}$.[14,15] Therefore, introducing oxidant $K_2S_2O_8$ not only can improve greatly faraday response of amiodarone, but also can eliminate efficiently the contamination of the polymerzation product of amiodarone toward the CPE.

Additionally, when non-ionic surfactant Triton X-100 was present in the HOAc-NaOAc buffer containing amiodarone, the peak current of the reduction wave at 0.3 V increased greatly, while the peak potential still was unchanged. The increase of the peak current might result from the increase of the solubility of amiodarone in aqueous solution due to the destroy of

low molecular weight aggregates of amiodarone dimer[27,28] and the formation of a complex between amiodarone and Triton X-100 via hydrogen bond, and the increase of adsorption on the CPE surface.[29,30]

Condition optimization

The combination of the catalysis caused by oxidant $K_2S_2O_8$ with the enhancement caused by surfactant Triton X-100 on faraday response of amiodarone was incorporated with adsorptive stripping voltammetric measurement. As a result, a high-performance CAdSV for the determination of amiodarone using CPE was developed. The experimental conditions were optimized. The 2.5th-order derivative technique was used in the voltammetric measurement because of its high sensitivity, good resolving power and low background current and allowance of using higher scan rate of potential. It was found that the peak current of the catalytic stripping peak increased with the increase of the pH value from 3.5 to 5.3. However, the peak current began to decrease when pH value was above 5.3. Otherwise, the peak potential was independent of pH value, demonstrating that the parallel catalytic wave resulted from subsequent oxidation of the intermediate free radical of amiodarone reduction by both $S_2O_8^{2-}$ and $SO_4^{-\bullet}$. The peak current increased gradually with the total concentration increasing of HOAc-NaOAc buffer (pH 5.3) from 0.1 to 0.2 mol•L^{-1}, and then began to decrease when the concentration was above 0.2 mol•L^{-1}, while the peak potential E_p never moved.

The peak current increased with the $K_2S_2O_8$ concentration increasing up to 2.0×10^{-2} mol•L^{-1}. When the $K_2S_2O_8$ concentration (w) was in the range of 2.0×10^{-2}—2.4×10^{-2} mol•L^{-1}, the peak current achieved a maximum value and remained nearly unchanged. The peak current of the catalytic wave was about 10 times higher than that of the corresponding reduction wave in the absence of $K_2S_2O_8$.

The effect of surfactants, cetyltrimethyl ammonium bromide (CTMAB), sodium lauryl sulfate (SLS) and Tween-80 and Triton X-100, was tested. Only Triton X-100 showed an obvious enhancement action on the peak current but no influence on the peak potential. When Triton X-100 concentration (w) was in the range of 0.0017%—0.0023%, the peak current reached maximum value, which was about 10 times higher than that in the absence of Triton X-100.

The peak current increased with potential increasing from −0.3 to 0 V. The peak current decreased with potential changing from 0 to 0.2 V. With accumulation time increasing up to 20 s, the peak current achieved the maximum value. The accumulation time of 30 s was satisfied with higher and lower levels of amiodarone. In addition, the peak current increased with the potential scan rate increasing, and at the same time, the peak form gradually became deformed.

In summary, the optimal conditions were as follows: 0.2 mol•L^{-1} HOAc-NaOAc buffer (pH 5.3) containing 0.02 mol•L^{-1} $K_2S_2O_8$ and 0.002% Triton X-100, an accumulation potential of 0 V, an accumulation time of 30 s and a potential scan rate of 0.3 V•s^{-1}. As shown in Figure 1, the 2.5th-order derivative catalytic stripping peak of amiodarone was well defined and easily measured.

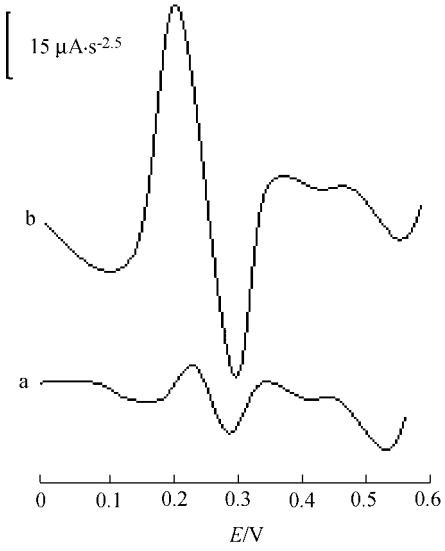

Figure 1 2.5th-order derivative CAdSV curves of (a) 1.0×10^{-8} mol•L^{-1} amiodarone in 0.2 mol•L^{-1} HOAc-NaOAc buffer (pH 5.3) and (b) 1.0×10^{-8} mol•L^{-1} amiodarone in 0.2 mol•L^{-1} HOAc-NaOAc buffer (pH 5.3) containing 0.02 mol•L^{-1} $K_2S_2O_8$ and 0.002% Triton X-100. Accumulation time: 30 s; accumulation potential: 0 V; Scan rate: 0.3 V•s^{-1}.

Validation

Linearity and sensitivity: Under the optimal conditions chosen, the 2.5th-order derivative peak current of the catalytic stripping wave at 0.3 V was linearly proportional to amiodarone concentration in the range of 2.0×10^{-10}—2.3×10^{-8} mol•L^{-1}, the linear regression equation was $e_p''/(\mu A\bullet s^{-2.5}) = (9.13 + 3.21)\times10^8$ $c/(\text{mol}\bullet L^{-1})$ (0.9979, $n=10$). The limit of detection (LOD$=3\ \sigma/s$, where σ is the standard deviation of the intercept and s is the slope of the calibration curve) was 1.5×10^{-10} mol•L^{-1}. The limit of quantitation (LOQ$=10\ \sigma/s$) was 5.1×10^{-10} mol•L^{-1}. These data confirmed that the proposed method possessed high sensitivity.

Intra- and inter-day precisions: In order to evaluate the accuracy and precision of the proposed method, analysis of standard amiodarone solutions at three levels, 8.0×10^{-10}, 4.2×10^{-9} and 1.8×10^{-8} mol•L^{-1}, was performed. Intra-assay accuracy and precision were obtained at each level by five replicate analyses in the same day. Inter-assay accuracy and precision were determined at each level over a period of five days by establishing calibration curves. The obtained data are summarized in Table 1, which proves that the proposed method showed good reproducibility.

Table 1 Inter-day and intra-day precision and accuracy of amiodarone

Amiodarone added/	Inter-assay (n=5)		Intra-assay (n=5)	
(10^{-10} mol•L^{-1})	Mean	RSD/%	Mean	RSD/%
8	7.96	1.5	8.16	3.6
42	42.98	1.8	40.89	2.4
180	180.5	2.2	178.6	−2.6

Specificity: The interference of common excipients, coexisting ions and others was examined. The solutions used for this purpose contained 8.0×10^{-8} mol•L^{-1} amiodarone and different amounts of interfering species. The tolerance limit for foreign species was taken as the largest amount yielding a relative error less than ± 5.0% for the determination of 8.0×10^{-8} mol•L^{-1} amiodarone. The results of the interference tests showed that 1000-fold Co^{2+}, Cu^{2+}, vitamin B1, serine, histidine, lysine, 500-fold Zn^{2+}, Fe^{3+}, Cd^{2+}, cystine, arginine, glutamate, 100-fold vitamin C, threonine, 50-fold, Fe^{2+}, Ni^{2+}, vitamin K3 and most common excipients present in pharmaceuticals did not interfere with the determination, which rendered the proposed method to have acceptable selectivity.

Pharmaceutical application: The proposed method was applied to the determination of amiodarone in pharmaceutical formulations. The amiodarone content of tablets (batch number 041002 and 030904) was determined directly using the calibration method. The recovery test was carried out by the standard addition method. The results are given in Table 2.

Table 2 Results for the determination and recovery test of amiodarone content in tablets[a]

Sample	Content[b]/	Amiodaront/(10^{-9} mol•L^{-1})		Recovery/%
	(mg/tablet)	Added	Found	
041002	200.6±0.3	0.80	0.79±0.01	98.8
		2.00	1.97±0.09	98.5
		4.00	4.06±0.04	101.5
030904	197.9±0.6	0.80	0.81±0.14	101.3
		2.00	2.04±0.11	102.0
		4.00	3.89±0.05	97.3

[a] Label amount 200 mg/tablet. [b] Mean value ±S.D (n=5).

Conclusion

Conveniently introducing the catalysis of oxidant into voltammetric determination using solid electrode is an efficient pathway to improve the analytical performance such as the high sensitivity owing to improving the faradiac response of analyte, the high reproducibility and the simple operation procedures owing to eliminating the deposition contamination from reduction product of analyte to solid electrodes. As an example, a CAdSV for the determination of amiodarone at CPE was developed by employing both the catalytic action of $K_2S_2O_8$ and the enhancement action of non-ionic surfactant Triton X-100. The low amiodarone level can be determined with this short accumulation time, which showed the good reproducibility without the contamination from amiodarone. The operation procedure is simple without any overlaborate renewal procedure of the solid electrode surface, and is easily realized by only adding both suitable oxidant and surfactant into supporting electrolyte. These capabilities allowed to develop simple, time saving, sensitive voltammetric method for organic substances of interest by using solid electrodes.

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Addition and Corrections

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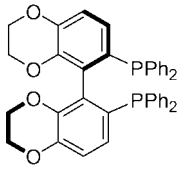
MA, Meng-Lin(马梦林); PENG, Zong-Hai(彭宗海); CHEN, Li(陈丽); GUO, Yu(郭妤); CHEN, Hua*(陈华); LI, Xian-Jun(李贤均). Synthesis of New MeO-BIPHEP-type Chiral Diphosphines by an Improved Way.

Page 1391, Scheme 1. The structure of *R*-SYNPHOS should be drawn as follows:



R-SYNPHOS

LIU, Jing-Yu(刘靖宇); ZHENG, Yi(郑毅); HU, Ning-Hai(胡宁海); LI, Yue-Sheng*(李悦生). Electron Effect of *p*-Substituent on Iron(II) and Cobalt(II) Pyridinebisimine Catalyst for Ethylene Polymerization

Page 1451, Conclusion should be as follows:

In summary, a series of iron and cobalt precatalysts were synthesized and characterized for ethylene polymerization. For iron precatalysts, not only the steric bulkiness but also the electronic effect of the substituents at the *o*- or *p*-position of the imines in pyridinebisimine ligands play an important role in the catalyst activities and the properties of the resulting polyethylenes. While concerning cobalt precatalyst, hindering effect of *p*-substituents is more important to determine catalyst activities and polymer mass than electronic effect.