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Screen-printed Electrode Modified with Magnetic Core-shell Nanoparticles for Detection of Chlorpromazine

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In the present study, magnetic core-shell manganese ferrite nanoparticles (MCMNP) were synthesized and used for construction of a magnetic core-shell manganese ferrite nanoparticles modified screen-printed carbon electrode (MCSNP-SPCE). Cyclic voltammetry was used to study the electrochemical behavior of chlorpromazine (CPZ) and its determination was conducted by applying square wave voltammetry (SWV). The MCSNP-SPCE in comparison with bare SPCE exhibited enhanced electrocatalytic activity toward the oxidation of CPZ. A single irreversible oxidation peak was observed at a potential of 500 mV and 630 mV on the MCSNP-SPCE and bare SPCE, respectively. Under the optimized conditions, the anodic peak current of CPZ recorded by SWV varies linearly with CPZ concentration in the range 0.25-60 μM with a detection limit of 0.08 μM. The MCSNP-SPCE was used for quantitative analysis of CPZ in tablet and urine samples and the results indicate the feasibility of the amperometric method for CPZ analysis in routine detection.

Keywords: Chlorpromazine determination, Magnetic core shell nanoparticles, Screen-printed carbon electrode

INTRODUCTION

The measurement of drugs is of great importance in pharmaceutical industry, biological studies, and medicine [1-5]. The measurement of trace amounts of drugs in biological samples such as serum and plasma of human blood and/or living tissues is carried out for diagnosing diseases, controlling the amount of drug, evaluating the stability as well as the toxicology of the drug, and investigating the therapeutic effects and complications of drug abuse [6].

Chlorpromazine (CPZ) is the most important compound in the large group of phenothiazine derivatives. It is widely used as a therapeutic agent for controlling excitement, agitation and other psychomotor disturbances in schizophrenic patients and reduces the manic phase of manic-depressive conditions. It is used to treat hyperkinetic states and aggression and is sometimes given in other psychiatric conditions for the control of anxiety and tension [7]. Since the anti-psychotic drugs are very active, they are usually administered at low daily dosages. In addition, CPZ is widely metabolized in the body. Therefore, the concentration of CPZ in plasma is low [8]. From bioanalytical and clinical points of view, highly sensitive, selective and accurate bioanalytical methods are needed to determine CPZ in biological fluids for obtaining optimum therapeutic concentrations and controlling its side effects [9].

Many methods have been reported to determine phenothiazines, including CPZ. Most of them imply optical-based methods, namely spectrophotometric [10], fluorimetric [11], and turbidimetric [12] procedures that regard several chemical transformations of CPZ [13]. High performance liquid chromatography (HPLC) [8], electrophoresis [14], voltammetric [15,16], coloumetric [17], polarographic [18] and spectroelectrochemical [19] procedures have been reported as well. However, many

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non-electrochemical methods like electrophoresis and chromatography have high sensitivity, but need expensive devices and accessories such as isolation system, temperature control; and they are time-consuming and costly. On the other hand, electrochemical methods are more advantageous due to their lower detection limits, higher sensitivity, higher selectivity, lower costs, simplicity, and the possibility direct measurement in biological media at shorter time intervals. Therefore, electrochemical methods based on anodic oxidation seem reasonable to determine drug concentrations. Due to the importance of measuring chlorpromazine hydrochloride, its measurement, using electrochemical and chemical methods, has been extensively considered [9,20,21].

The screen-printed electrodes (SPEs) have been designed especially for miniaturization of electrochemical analytical systems [22]. SPEs are highly-versatile, easy to use, cost-effective analytical tools, also suitable to miniaturization [23]. Furthermore, a screen printed electrode avoids the cleaning process, unlike conventional electrodes such as a glassy carbon electrode (GCE) [24].

Nowadays, it continues to be of interest in the developments of new materials capable to change the electrode surface with better analytical properties, including graphene, nanoparticles, and carbon nanotubes [25-36]. Among them, nanosized metal particle modified electrodes have emerged as a promising alternative for the electroanalysis of organic and inorganic compounds [37-41].

Metal nanoparticles have some distinct advantages such as higher mass transport, lower influence of the solution resistance, low detection limit, and better signal-to noise ratio over the conventional electrodes [42-44].

Metals in the nanometer range provide three important functions for electroanalysis: the roughening of the conductive sensing interface, catalytic properties, and conductivity properties [45]. From both fundamental and industrial points of view, many different synthetic procedures have been developed for the preparation of metal nanoparticles (NPs).

In the present work, we synthesized magnetic core-shell manganese ferrite nanoparticles (MCSNP) [46] and screen printed carbon electrodes were modified with MCSNP. To the best of our knowledge, no study has been reported so far on the determination of chlorpromazine by using MCSNP/SPCE.

EXPERIMENTAL

Apparatus and Chemicals

The electrochemical measurements were performed with an Autolab potentiostat/galvanostat (PGSTAT 302N, Eco Chemie, the Netherlands). The experimental conditions were controlled with General Purpose Electrochemical System software. Screen printed electrodes were purchased from Italsens Co. A Metrohm 710 pH meter was used for pH measurements.

Chlorpromazine hydrochloride and all the other reagents were of analytical grade and were obtained from Merck (Darmstadt, Germany). The buffer solutions were prepared from orthophosphoric acid and its salts in the pH range of 2.0-9.0. Magnetic core-shell manganese ferrite nanoparticles were synthesized in our laboratory as reported previously [46]. Figure 1 illustrates a typical SEM of MCSNP.

Preparation of the Electrode

The bare screen-printed electrode was coated with MCSNP as follows. A stock solution of MCSNP in 1 ml aqueous solution was prepared by dispersing 1 mg MCSNP with ultrasonication for 1 h, and a 2 µl aliquot of the MCSNP/H_2O suspension solution was casted on the carbon working electrodes, waiting until the solvent was evaporated in room temperature.

Preparation of Real Samples

Five tablets of chlorpromazine (labeled 25 mg per each tablet) were completely ground and homogenized, 200 mg of this powder was accurately weighed and dissolved with ultrasonication in 10 ml of water. Finally the mixture was filtered and the clear filtrate was transferred into a 50 ml volumetric flask and diluted to the mark with using 0.1 M PBS with pH 7.0. Finally, a suitable volume of the resultant solution was transfer to electrochemical cell and the resulting solution was used for the analysis of chlorpromazine. The sample was spiked with different amounts of chlorpromazine and contents were analyzed by using the standard addition method in order to prevent any

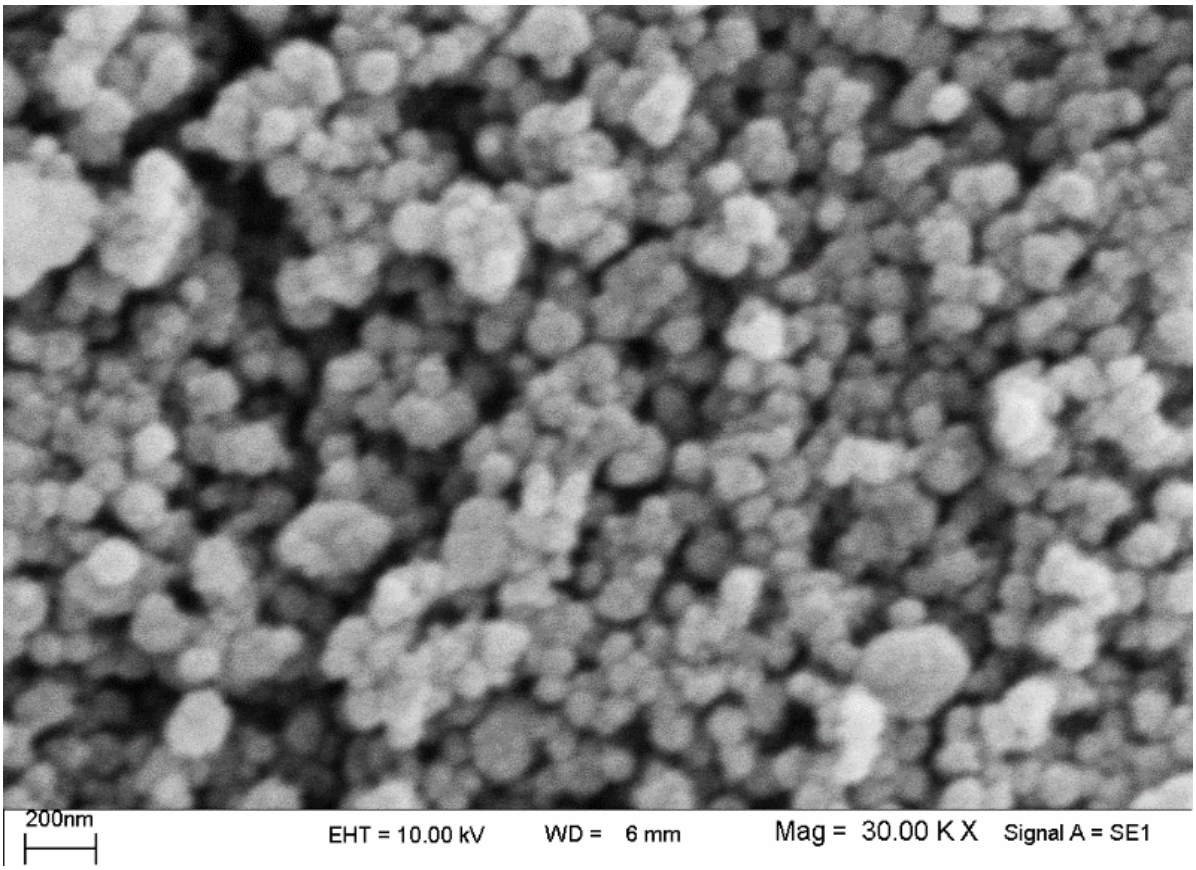

Fig. 1. Scanning electron microscope image of magnetic core-shell manganese ferrite nanoparticles.

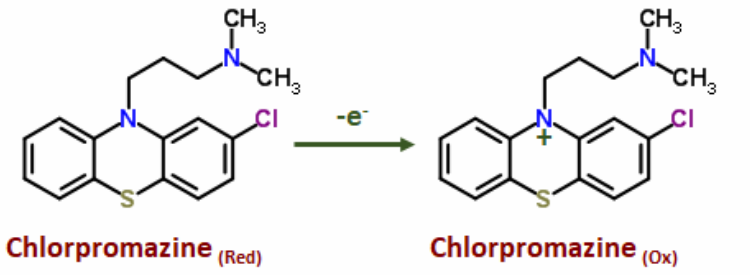

Fig. 2. Mechanism for oxidation of chlorpromazine.

matrix effect. The amount of unknown chlorpromazine in the tablet can be detected by extrapolating the plot.

Urine samples were stored in a refrigerator immediately after collection. Ten milliliters of the sample was centrifuged for 10 min at 3000 rpm. The supernatant was filtered out using a 0.45 µm filter. Then, different volume of the solution was transferred into a 25 ml volumetric flask and diluted to the mark with PBS (pH 7.0). The diluted urine sample was spiked with different amounts of chlorpromazine. The chlorpromazine contents were

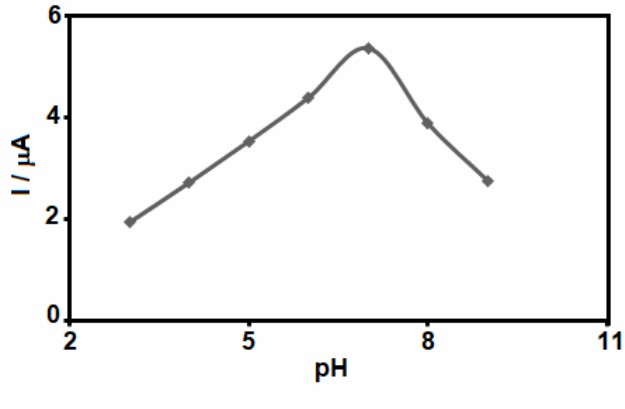

Fig. 3. Peak current of the MCSNP/SPCE in the presence of 15.0 µM chlorpromazine at various buffered pHs.

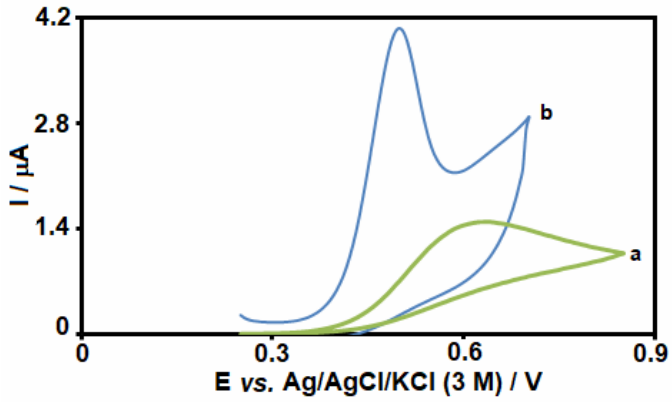

Fig. 4. Voltammograms of (a) unmodified SPE and (b) MCSNP/SPCE in the presence of 10.0 µM chlorpromazine at pH 7 (at 50 mV s^{-1}).

analyzed by the proposed method using the standard addition method in order to prevent any matrix effect.

RESULTS AND DISCUSSION

The pH Effect

In general, pH is one of the variables that commonly influences on the current and shape of voltammograms. Therefore, pH optimization of the solution seems to be necessary in order to obtain the best results for electrooxidation of chlorpromazine. Thus the electrochemical behaviors of chlorpromazine were studied in 0.1 M PBS in different pH values (3.0-9.0) at the surface of MCSNP/SPCE. A stable peak obtained for chlorpromazine in different pH values. The results were showed that, oxidation peak potential of the chlorpromazine at MCSNP/SPCE is independent of pH, which means that the voltammetric behavior of chlorpromazine is not a proton transfer process under experimental conditions (Fig. 2). Furthermore, the peak current was found to be dependent on the pH and higher peak currents are observed at pH 7.0. Therefore, phosphate buffer with pH 7.0 was selected and used as the supporting electrolyte in all voltammetric determinations (Fig. 3).

Electrochemical Behavior of Chlorpromazine at the Surface MCSNP/SPCE

Figure 4 depicts the CV responses for the electro-

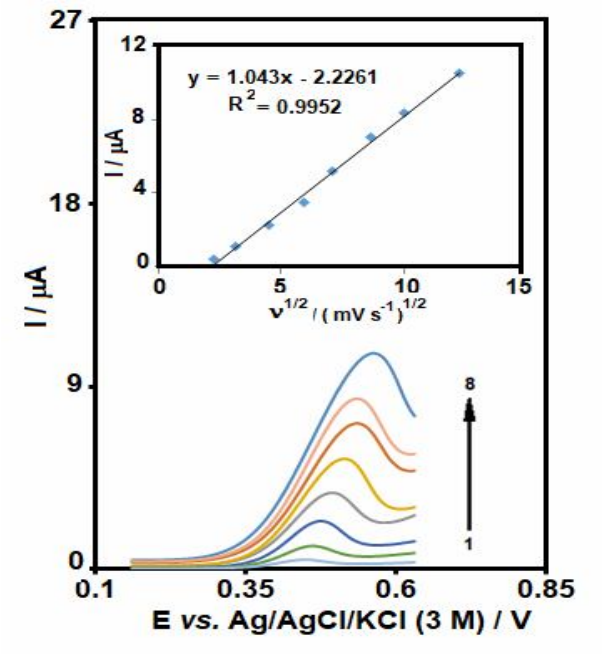

Fig. 5. LSVs of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing 5.0 µM chlorpromazine at various scan rates; numbers 1-8 correspond to 5, 10, 20, 35, 50, 75, 100 and 150 mV s^{-1}, respectively. Inset: Variation of anodic peak current *vs*. square root of scan rate.

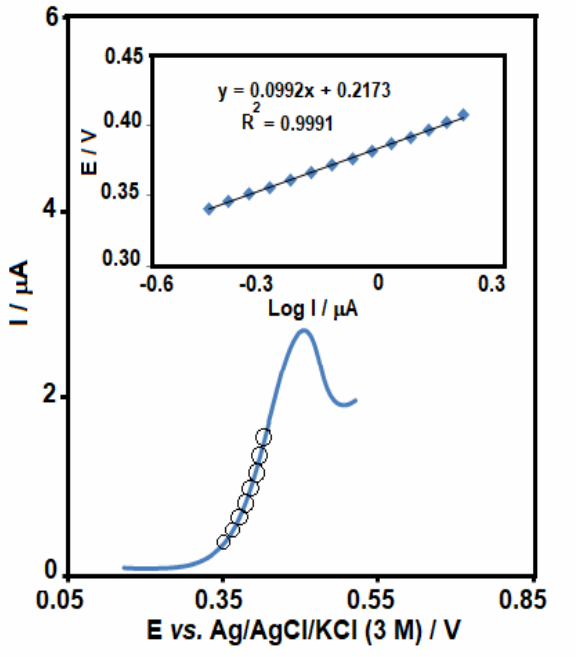

Fig. 6. Tafel plot derived from LSV of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing 5.0 µM chlorpromazine at scan rate of 10 mV s^{-1}.

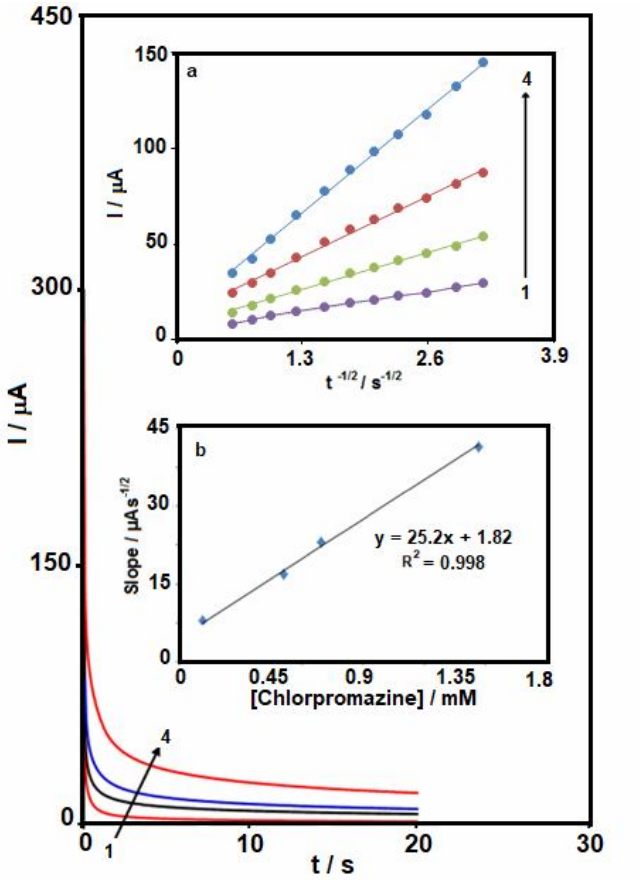

Fig. 7. Chronoamperograms obtained at MCSNP/SPCE in 0.1 M PBS (pH 7.0) for different concentration of chlorpromazine. The numbers 1-4 correspond to 0.1, 0.5, 0.75 and 1.5 mM of chlorpromazine. Insets: Plots of I *vs*. $t^{-1/2}$ obtained from chronoamperograms 1-4 (a), and Plot of the slope of the straight lines against chlorpromazine concentration (b).

oxidation of 10.0 µM chlorpromazine at an unmodified SPCE (curve a) and MCSNP/SPCE (curve b). The peak potential due to the oxidation of chlorpromazine occurs at 500 mV, which is about 130 mV more negative than that of unmodified SPCE.

Also, MCSNP/SPCE shows much higher anodic peak current for the oxidation of chlorpromazine compared to unmodified SPCE, indicating that the modification of unmodified SPCE with MCSNP has significantly improved the performance of the electrode toward chlorpromazine oxidation.

Effect of Scan Rate

The effect of potential scan rates on the oxidation current of chlorpromazine (Fig. 5) have been studied. The results showed that increasing in the potential scan rate induced an increase in the peak current. In addition, the oxidation processes are diffusion controlled as deduced from the linear dependence of the anodic peak current (I_p) on the square root of the potential scan rate ($\upsilon^{1/2}$).

Tafel plot was drawn from data of the rising part of the current voltage curve recorded at a scan rate of 10 mVs^{-1} for chlorpromazine (Fig. 6).

This part of voltammogram, known as Tafel region, is affected by electron transfer kinetics between substrate (chlorpromazine) and MCSNP/SPCE. Tafel slope of 0.0992 V was obtained which agree well with the involvement of one electron in the rate determining step of the electrode

process [47] assuming charge transfer coefficients, $\alpha = 0.4$ for chlorpromazine.

Chronoamperometric Measurements

Chronoamperometric measurement of chlorpromazine at MCSNP/SPCE was carried out by setting the working electrode potential at 0.7 V *vs*. Ag/AgCl/KCl (3.0 M) for the various concentrations of chlorpromazine (Fig. 7) and in PBS (pH 7.0). For electroactive materials (chlorpromazine) with a diffusion coefficient of D, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation [47]:

$$I = nFAD^{1/2} C_b \pi^{-1/2} t^{-1/2} \quad (1)$$

Where D and C_b are the diffusion coefficient ($cm^2\ s^{-1}$) and the bulk concentration (mol cm^{-3}), respectively. Experimental plots of I *vs*. $t^{-1/2}$ were employed, with the best fits for different concentrations of chlorpromazine (Fig. 7a). The slope of the resulting straight lines were then plotted *vs*. chlorpromazine (Fig. 7b) concentrations. From the resulting slope and Cottrell equation the mean value of the D was found to be 2.17×10^{-6} $cm^2\ s^{-1}$ for chlorpromazine.

Calibration Plots and Limits of Detection

The electro-oxidation peak current of chlorpromazine at the surface of the MCSNP/SPCE can be used for determination of chlorpromazine in solution. Since, square wave voltammetry (SWV) has the advantage of an increase in sensitivity and better characteristics for analytical applications, therefore, SWV experiments were performed using MCSNP/SPCE in 0.1 M PBS containing various concentrations of chlorpromazine (Fig. 8). The results show the electrocatalytic peak currents of chlorpromazine oxidation at the surface of MCSNP/SPCE was linearly dependent on the chlorpromazine concentrations, over the range of 0.25×10^{-6}-6.0×10^{-5} M (with a correlation coefficient of 0.9985) and the detection limit (3σ) was obtained 0.8×10^{-7} M.

Interference Study

We investigated the effect of different species on measuring the 20 μM CPZ. The tolerance limit was adjusted for the concentration of species with ±5% error in the determination. Based on the obtained results, Mg^{2+}, Fe^{2+}, Co^{2+}, Cl^-, SO_4^{2-}, Br^-, glycine, glucose, sucrose, fructose, aspartic acid, urea, uric acid, acetaminophen, cysteine and ascorbic acid did not show interference in determination of chlorpromazine.

Real Sample Analysis

Finally, MCSNP/SPCE was applied for determination of chlorpromazine in chlorpromazine tablet, and urine samples. For this purpose, the determination of chlorpromazine in the real samples were carried out by using standard addition method to prevent any matrix effects. The results are shown in Table 1. Also, the recovery of chlorpromazine from samples spiked with known amounts of chlorpromazine was studied. The results were showed that, the added chlorpromazine was quantitatively recovered from the real samples. These results demonstrate the applicability of the MCSNP/SPCE for determination of chlorpromazine in the real samples. Also, the reproducibility of the method was demonstrated by the mean relative standard deviation (RSD).

The amount of chlorpromazine in tablet was found to be 25.2 mg per each tablet. It was found that there is no significant difference between the result obtained by the MCSNP/SPCE and the nominal value on the tablet label (25.0 mg). The t-test was applied to the results and showed that there was no significant difference at the 95% confidence level.

CONCLUSIONS

In this work, employing magnetic core shell nanoparticles as modifier in modification of SPCEs, a novel sensor has been developed that provides a sensitive method for the determination of chlorpromazine. The proposed protocol demonstrated herein a novel, simple, portable, inexpensive and easy-to-use fabrication method for the measurement of chlorpromazine concentration in tablet and urine samples with good analytical performance. Due to the unique properties of magnetic core shell nanoparticles, the sensor exhibited remarkable electrochemical activity toward the oxidation of chlorpromazine. Under optimized conditions, square wave voltammetry exhibited linear

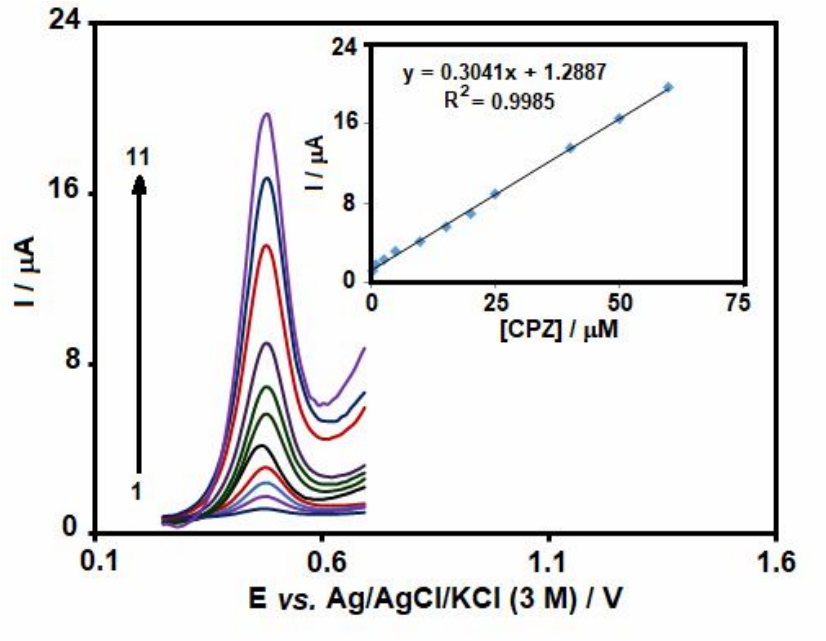

Fig. 8. SWVs of MCSNP/SPCE in 0.1 M PBS (pH 7.0) containing different concentrations of chlorpromazine (0.25, 1.0, 2.5, 5.0, 10.0, 15.0, 20.0, 25.0, 40.0, 50.0 and 60.0 µM). Inset: The plot of the peak current as a function of chlorpromazine concentration in the range of 0.25-60 µM.

Table 1. The Application of MCSNP/SPE for Determination of Chlorpromazine in Real samples (n = 5)

Sample	Spiked (µM)	Found (µM)	Recovery (%)	R.S.D. (%)
Chlorpromazine tablet	0.0	15.1	-	3.1
	10.0	25.4	103.0	2.9
	20.0	35.3	101.0	2.6
	30.0	44.7	98.7	2.8
Urine	0	ND[a]	-	-
	10.0	10.2	102.0	2.7
	20.0	19.7	98.5	3.4
	30.0	29.6	98.7	3.1

[a]Not detected.

dynamic ranges from 0.25-60 μM with detection limit of 0.08 μM.

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