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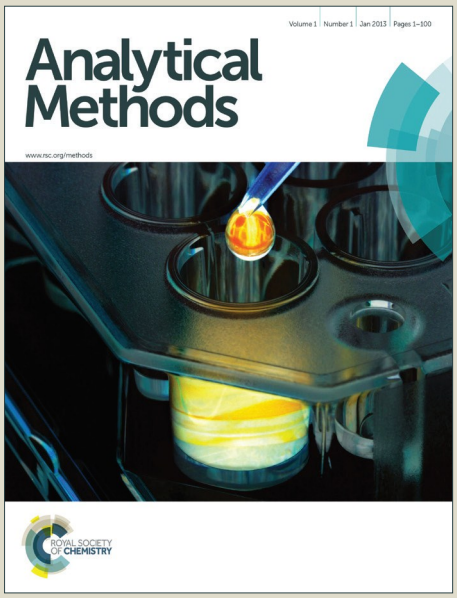

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Magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite modified carbon paste electrode for amplified electrochemical sensing of amlodipine and hydrochlorothiazide

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A novel carbon paste electrode modified with magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite and an ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) was fabricated. The electrochemical study of the modified electrode, as well as its efficiency for simultaneous voltammetric oxidation of amlodipine and hydrochlorothiazid is described. The electrode was also employed to study the electrochemical oxidation of amlodipine and hydrochlorothiazide, using cyclic voltammetry, chronoamperometry and square wave voltammetry as diagnostic techniques. Square wave voltammetry exhibited linear dynamic ranges from 2.5×10^{-7} to 5.0×10^{-4}M and 1.0×10^{-6} to 6.0×10^{-4} M for amlodipine and hydrochlorothiazide respectively. Finally the modified electrode was used for determination of amlodipine and hydrochlorothiazide in real samples.

Keywords: Amlodipine, Hydrochlorothiazide, Core–shell nanocomposite, Drug Analysis, Ionic liquids, Voltammetry

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1. Introduction

Amlodipine and hydrochlorothiazide (Scheme 1) are two drugs widely used for the treatment of hypertension, used separately or together in a combined pharmaceutical formulation.[1, 2] Amlodipine besylate is a dihydropyridine type with calcium antagonist activity.[3-5] It inhibits the transmembrane influx of calcium ions into vascular smooth muscle and cardiac muscle to protect the target organs. Moreover, it may cross the blood brain barrier and is used in cerebral ischaemia.[6, 7] On the other hand, hydrochlorothiazide is a diuretic drug belonging to the thiazide class, which increases the renal excretion of water and electrolytes.[8-12]

As it is known, treating patients with an amlodipine and hydrochlorothiazide combination therapy regimen, each medication with a different mechanism of action, is more effective at lowering blood pressure than each drug alone.[13] Due to the frequency that amlodipine and hydrochlorothiazide are prescribed, it is very interesting the development of simple, sensitive and accurate analytical method for simultaneous determination of both compounds in pharmaceuticals, especially for quality control purpose.

Compared with other methods, electrochemical methods offer the practical advantages involving operation simplicity, low expense of instrument, suitability for real-time detection and lower sensitivity to matrix effects in comparison with chromatographic methods. Also, they represent the useful alternative methods widely applied in analysis of pharmaceuticals. In addition, there is the possibility of analysis of colored or solutions with suspended solids.[14-19] In comparison with other electrodes, carbon paste electrodes (CPEs) have gained considerable attention.[20] The bare CPE is a mixture of an electrically conducting graphite powder and a traditional liquid (usually paraffin). But, the sensitivity of the bare CPE is relatively poor for trace assay of these species. In order to overcome these problem, a fascinating and effective way is to modify it by mixing with some other unique substances.[21-23]

Recently room temperature ionic liquids (RTILs) have received great attention due to their specific characteristics such as negligible vapor pressure, high polarity, highly solvating, non-coordinating and non-flammable, uses as acidic catalysts in many

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reactions by reason of the tunable acidity.[24] As a novel "green" solvent, RTILs have been used in synthetic chemistry, material science, catalytic chemistry and electrochemistry. In the field of electrochemistry, RTILs possess the characteristics of wider electrochemical window and higher ionic conductivity, so they can be used as the supporting electrolyte or the modified material for electrochemical measurements.[25, 26]

Nanostructures carbon materials, especially carbon nanotubes (CNTs), are one of the most promising supporting materials for surface modification of electrodes, due to their unique properties, such as good biocompatibility, high surface-to-volume ratio, enhanced magnetic and electrical properties.[27-31] Currently, carbon nanotubes/metal oxides have been widely reported. Metal oxides are active and durable electrocatalysts for biosensors. Among metal oxide, Fe_3O_4 has attracted growing interest in recent years, due to its good biocompatibility, strong superparamagnetic property, low toxicity and easy preparation, which is widely utilized in various fields.[32, 33] Therefore CNTs with magnetic nanomaterials are one of the most useful nanocomposites, which incorporate the features of both CNTs and magnetic nanomaterials. However, an inert silica (SiO_2) nanoparticle coating on the surface of Fe_3O_4 nanoparticles prevents their aggregation, improves their chemical stability, and provides better protection against toxicity.[34, 35]

In the present work, we describe the preparation of a new carbon paste electrode modified with an ionic liquid and magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite (ILFSCNPE) and investigate its performance for the determination of amlodipine in the presence of hydrochlorothiazide in aqueous solutions. Finally the modified electrode was used for determination of amlodipine and hydrochlorothiazide in real samples.

2. Experimental

2.1 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 (GPES) software. A conventional three electrode cell was used at 25 ± 1 °C. An

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Ag/AgCl/KCl (3.0 M) electrode (Azar Electrode, Urmia, Iran), a platinum wire (Azar Electrode, Urmia, Iran), and ILFSCNPE were used as the reference, auxiliary and working electrodes, respectively. A Metrohm 710 pH meter (The Netherlands) was used for pH measurements.

Amlodipine, hydrochlorothiazide and all of 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. Ionic liquid (n-hexyl-3-methylimidazolium hexafluoro phosphate) was purchased from Sigma Aldrich Co (USA).

2.2. Synthesis of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite

The preparation process of Fe_3O_4@SiO_2/MWCNT nanocomposite is illustrated in Scheme 2. As it shows, the carboxylated MWCNTs (MWCNTs–COOH) were prepared by refluxing the MWCNTs in a mixture of concentrated sulfuric acid and nitric acid (3:1 v/v ratio) at 70 °C for 6 h. After cooling to room temperature the mixture was filtered and washed with double distilled water until the pH of the filtrate became ~7 and finally dried at 60 °C overnight. About 0.1 g of MWCNTs–COOH was dissolved in 70 mL of water by ultrasonic irradiation (Sono swiss SW3-H, 38 kHz, Switzerland) for 20 min. The mixture was further stirred vigorously for 30 min at 60 °C. Then 177 mg of $FeCl_3 \cdot 6H_2O$ was added under stirring. After the mixture was stirred vigorously for 30 min under N_2 atmosphere, 95 mg of $FeSO_4 \cdot 7H_2O$ was added and keeping it stirred under N_2 atmosphere for 30 min. At last 30 mL of 6% NH_4OH aqueous solution was added into the mixture drop by drop at 60 °C during 1 h and reacted for another 2 h. N_2 atmosphere was used during the reaction to prevent critical oxidation. The reaction mixture was then centrifuged, washed with double distilled water and dried. The obtained black precipitate was Fe_3O_4/MWCNT nanoparticles and was ready for use. Core–shell Fe_3O_4@SiO_2/MWCNT nanocomposites were prepared by growing silica layers onto the surface of the Fe_3O_4/MWCNTs as described by Lu et al..[36] 25 mL ethanol, 1 mL water, 1 mL ammonium hydroxide and 150 µL of TEOS were added in a 250 mL three neck flask in a 40 °C water bath. Fe_3O_4/MWCNTs were added to the above solution under

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mechanical stirring. Aliquots of the mixture were taken out after 12 h by centrifugation and washed with water and vacuum-dried at 60 °C overnight.

2.3. Preparation of the electrode

To obtain the best conditions in the preparation of the ILFSCNPEs, we optimized the ratio of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite, IL and graphite powder. The results of our studied showed that the maximum peak current intensity of amlodipine and hydrochlorothiazide could be obtained at the surface of ILFSCNPE with optimum ratio of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite, IL and graphite powder.

ILFSCNPE was prepared by mixing 0.04 g of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite with 0.96 g graphite powder and approximately, ~ 0.8 mL of ionic liquids with a mortar and pestle. The paste was then packed into the end of a glass tube (ca. 3.4 mm i.d. and 15 cm long). A copper wire inserted into the carbon paste provided the electrical contact.

For comparison, ionic liquid / carbon paste electrode in the absence of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite (ILCPE), magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite carbon paste electrode (FSCNPE) consistent of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite and paraffin oil, and bare carbon paste electrode (CPE) consisiting of graphite powder and paraffin oil were also prepared in the same way.

3. Result and discussion

3.1. FT-IR and SEM characterization

Fig. 1 shows the FT-IR spectra of (a) MWCNTs–COOH (b) Fe_3O_4/ MWCNTs and (c) Fe_3O_4@SiO_2/MWCNTs. In Fig. 1(a) the peaks at 1636 and 1381 cm^{-1} correspond to C=O and C–O stretching, respectively. The two weak peaks at 2928 and 2850 cm^{-1} correspond to the –CH stretching mode and a broad band peak at 3439 cm^{-1} is attributed to the

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COOH groups onto the external surface of MWCNTs.[37] In addition, in Fig. 1(b) the peak at 605 cm^{-1} is the stretching vibration due to the interactions of Fe–O–Fe in Fe_3O_4. Compared with the two spectra (b and c), the existence of the characteristic Si–O–Si peak at 1080 cm^{-1} in Fig. 1(c) is direct evidence to verify the formation of the silica shell.[38]

The surface morphologies of (a) MWCNTs–COOH (b) Fe_3O_4/ MWCNTs and (c) Fe_3O_4@SiO_2/MWCNTs were investigated by SEM and depicted in Fig. 2.

3.2 Electrochemical behavior of amlodipine and hydrochlorothiazide at the surface of various electrodes

The electrochemical behavior of amlodipine and hydrochlorothiazide are dependent on the pH value of the aqueous solution. Therefore, pH optimization of the solution seems to be necessary in order to obtain the best sensitivity and also the best resolution of two compounds oxidation peaks. Thus the electrochemical behaviors of amlodipine and hydrochlorothiazide were studied in 0.1 M PBS with different pH values ($2.0 < pH < 9.0$) at the surface of a ILFSCNPE using SWV. It was found that the best sensitivity and also the best resolution of two compounds oxidation peaks were obtained under neutral conditions than in an acidic or basic medium. This appears as a gradual growth in the anodic peak current and simultaneous the best resolution of two compounds oxidation peaks. Thus, pH 7.0 was chosen as the optimum pH for the determination of amlodipine and hydrochlorothiazide at the surface of an ILFSCNPE.

Fig. 3A and 3B display cyclic voltammetric responses from the electrochemical oxidation of 150.0 μM amlodipine (A) and 100.0 μM hydrochlorothiazide (B) at the surface of ILFSCNPE (curve d), ILCPE (curve c), FSCNPE (curve b) and bare CPE (curve a) respectively. The results showed that the oxidation of amlodipine and hydrochlorothiazide were very weak at the surface of the bare CPE, but the presence of ILs in CPE could enhance the peak current and decrease the oxidation potential (decreasing the overpotential). Substantial negative shifts of the oxidation potentials for amlodipine and hydrochlorothiazide and dramatic increase of the currents indicate the catalytic ability of ILFSCNPE (curve d) and ILCPE (curve c) to amlodipine and hydrochlorothiazide oxidation. The results showed that the combination of magnetic

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core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite and the ionic liquid (curve d) definitely improved the characteristics of amlodipine and hydrochlorothiazide oxidation. However, ILFSCNPE shows much higher anodic peak current for the oxidation of amlodipine and hydrochlorothiazide compared to ILCPE, indicating that the combination of magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite and ionic liquids has significantly improved the performance of the electrode toward amlodipine and hydrochlorothiazide oxidation. Table 1 shows the electrochemical characteristics of amlodipine and hydrochlorothiazide oxidation at the surface of various electrode at pH 7.0.

3.3. Effect of scan rate

The effect of potential scan rates on the oxidation current of amlodipine (Fig. 4A) and hydrochlorothiazide (Fig. 4B) have been studied using CV. The results showed that increasing in the potential scan rate induced an increase in the peak current. In addition, the oxidation process is diffusion controlled as deduced from the linear dependence of the anodic peak current (I_p) on the square root of the potential scan rate ($\nu^{1/2}$).[39]

In order to obtain information on the rate-determining step, Tafel slope *b*, was determined using E vs. log I plots. The Tafel slope of 0.19 V and 0.13 V obtained in these cases agree well with the involvement of one electron in the rate determining step of the electrode process, assuming a charge transfer coefficients of α=0.69 and α=0.55 for amlodipine and hydrochlorothiazide respectively.[39]

3.4. Chronoamperometric measurements

Chronoamperometric measurements of amlodipine (Fig. 5A) and hydrochlorothiazide (Fig. 5B) at ILFSCNPE were carried out by setting the working electrode potential at 0.9 V and 0.95 V vs. Ag/AgCl/KCl (3.0 M) for the various concentrations of amlodipine and hydrochlorothiazide in PBS (pH 7.0) respectively. For electroactive materials (amlodipine or hydrochlorothiazide in this case) with diffusion coefficients of D, the current observed for the electrochemical reaction at the mass transport limited condition is described by the Cottrell equation[39]:

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

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 amlodipine and hydrochlorothiazide. The slopes of the resulting straight lines were then plotted vs. amlodipine and hydrochlorothiazide concentrations. From the resulting slopes and Cottrell equation the mean values of the D were found to be 1.4×10^{-6} and 1.19×10^{-6} cm^2/s for amlodipine and hydrochlorothiazide respectively.

3.5. Calibration plots and limits of detection

The peak currents of amlodipine (Fig. 6A) and hydrochlorothiazide (Fig. 6B) oxidation at the surface of the modified electrode can be used for determination of amlodipine and hydrochlorothiazide in solution. Therefore, square wave voltammetry (SWV) experiments were done for different concentrations of amlodipine and hydrochlorothiazide. The oxidation peak currents of amlodipine and hydrochlorothiazide at the surface of the modified electrode were proportional to the concentrations of the amlodipine and hydrochlorothiazide within the ranges 2.5×10^{-7} to 5.0×10^{-4} M and 1.0×10^{-6} to 6.0×10^{-4} M with detection limits (3σ) of 0.015±0.002 μM and 0.0085± 0.0018 μM for amlodipine and hydrochlorothiazide respectively. These values are comparable with values reported by other research groups for determination of amlodipine and hydrochlorothiazide at the surface of modified electrodes (see Table 2).

3.6. Simultaneous determination of amlodipine and hydrochlorothiazide

To our knowledge, no paper has used the ILFSCNPE for simultaneous determination of amlodipine and hydrochlorothiazide and this is the first report for simultaneous determination of amlodipine and hydrochlorothiazide using ILFSCNPE. Determinations

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of two compounds were performed by simultaneously changing the concentrations of amlodipine and hydrochlorothiazide, and recording the SWVs (Fig. 7). The voltammetric results showed well-defined anodic peaks at potentials of 710 and 830 mV, corresponding to the oxidation of amlodipine and hydrochlorothiazide, respectively, indicating that simultaneous determination of these compounds is feasible at the ILFSCNPE as shown in Fig. 7.

3.7. The repeatability and stability of ILFSCNPE

The longterm stability of the ILFSCNPE was tested over a 3-week period. When CVs were recorded after the modified electrode was stored in atmosphere at room temperature, the peak potentials for amlodipine and hydrochlorothiazide oxidation were unchanged and the current signals showed less than 2.6% decrease relative to the initial response. The antifouling properties of the modified electrode toward amlodipine and hydrochlorothiazide oxidation and their oxidation products were investigated by recording the CVs of the modified electrode before and after use in the presence of amlodipine and hydrochlorothiazide. CVs were recorded in the presence of amlodipine or hydrochlorothiazide after having cycled the potential 15 times at a scan rate of 50 mV s^{-1}. The peak potentials were unchanged and the currents decreased by less than 2.4%. Therefore, at the surface of ILFSCNPE, not only the sensitivity increase, but the fouling effect of the analyte and its oxidation product also decreases.

3.8. Interference study

The influences of various foreign species on the determination of amlodipine and hydrochlorothiazide were investigated. The tolerance limit was taken as the maximum concentration of the foreign substances which caused an approximately ±5 % relative error in the determination. Based on the obtained results uric acid, ascorbic acid, dopamine, epinephrine, norepinephrine, methyldopa, carbidopa, levodopa, droxidopa, isoproterenol, caffeine and glucose did not show interference in the determination of amlodipine and hydrochlorothiazide.

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3.9. Real sample analysis

In order to evaluate the analytical applicability of the proposed method, also it was applied to the determination of amlodipine in amlodipine tablet and urine samples (Table 3) and hydrochlorothiazide in hydrochlorothiazide tablet and urine samples (Table 4). Human urine samples were provided by a volunteer for analysis. Informed consent was obtained for any experimentation with human subjects. Satisfactory recovery of the experimental results was found for amlodipine and hydrochlorothiazide. The reproducibility of the method was demonstrated by the mean relative standard deviation (R.S.D.).

4. Conclusion

In the present study, a magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite / ionic liquid modified carbon paste electrode was constructed. The modified electrode was applied for amlodipine and hydrochlorothiazide determination. Excellent features, like a wide linear range, low detection limit, high reproducibility and repeatability and long time stability proved the successful application of this sensor for the determinations of amlodipine and hydrochlorothiazide. The SWV currents of amlodipine and hydrochlorothiazide were proportional to the concentrations of the amlodipine and hydrochlorothiazide within the ranges 2.5×10^{-7} to 5.0×10^{-4} M and 1.0×10^{-6} to 6.0×10^{-4} M with detection limits (3σ) of 1.5×10^{-7} M and 8.5×10^{-8} M for amlodipine and hydrochlorothiazide respectively. Finally, this method was used for the determination of amlodipine and hydrochlorothiazide in some real samples.

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Legend for the figures:

Fig. 1. FT-IR spectra of (a) MWCNTs–COOH, (b) Fe_3O_4/MWCNTs and (c) Fe_3O_4@SiO_2/MWCNTs.

Fig. 2. SEM image for (A) MWCNTs–COOH, (B) Fe_3O_4/MWCNTs and (C) Fe_3O_4@SiO_2/MWCNTs.

Fig. 3. (A) CVs of a) CPE, b) FSCNPE, c) ILCPE and d) ILFSCNPE in the presence of 150.0 μM amlodipine at pH 7.0, respectively. (B) CVs of a) CPE, b) FSCNPE, c) ILCPE and d) ILFSCNPE in the presence of 100.0 μM hydrochlorothiazide at a pH 7.0, respectively. In all cases the scan rate was 50 mV s^{-1}.

Fig. 4. (A) CVs of ILFSCNPE in 0.1 M PBS (pH 7.0) containing 250.0 μM amlodipine at various scan rates; numbers 1-10 correspond to 10, 20, 40, 60, 80, 100, 200, 400, 600 and 800 mV s^{-1}, respectively. Inset: Variation of anodic peak current *vs*. square root of scan rate. (B) CVs of ILFSCNPE in 0.1 M PBS (pH 7.0) containing 150.0 μM hydrochlorothiazide at various scan rates; numbers 1-10 correspond to 10, 20, 40, 60, 80, 100, 300, 500, 700 and 900 mV s^{-1}, respectively. Inset: Variation of anodic peak current *vs*. square root of scan rate.

Fig. 5. (A) Chronoamperograms obtained at ILFSCNPE in 0.1 M PBS (pH 7.0) for different concentrations of amlodipine. The numbers 1–6 correspond to 0.1, 0.25, 0.5, 0.75, 1.25 and 2.0 mM of amlodipine. Insets: (A) Plots of I vs. $t^{-1/2}$ obtained from chronoamperograms 1–6. (B) Plot of the slope of the straight lines against amlodipine concentrations. (B) Chronoamperograms obtained at ILFSCNPE in 0.1 M PBS (pH 7.0) for different concentrations of hydrochlorothiazide. The numbers 1–4 correspond to 0.1, 0.25, 0.5 and 1.0 mM of hydrochlorothiazide. Insets: (A) Plots of I vs. $t^{-1/2}$ obtained from chronoamperograms 1–4. (B) Plot of the slope of the straight lines against hydrochlorothiazide concentrations.

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Fig. 6. (A) SWVs of ILFSCNPE in 0.1 M PBS (pH 7.0) containing different concentrations of amlodipine. Numbers 1-13 correspond to 0.25, 1.0, 5.0, 10.0, 20.0, 40.0, 60.0, 80.0, 100.0, 200.0, 300.0, 400.0 and 500.0 μM of amlodipine. Inset shows the plots of the peak current as a function of amlodipine concentrations in the range of 0.25-400.0 μM. (B) SWVs of ILFSCNPE in 0.1 M PBS (pH 7.0) containing different concentrations of hydrochlorothiazide. Numbers 1-15 correspond to 1.0, 2.5, 5.0, 7.5, 10.0, 20.0, 40.0, 60.0, 80.0, 100.0, 200.0, 300.0, 400.0, 500.0 and 600.0 μM of amlodipine. Inset shows the plots of the peak current as a function of hydrochlorothiazide concentrations in the range of 1.0-600.0 μM.

Fig. 7. SWVs of ILFSCNPE in 0.1 M PBS (pH 7.0) containing different concentrations of amlodipine and hydrochlorothiazide in μM, from inner to outer: 10.0+ 1.0, 60.0 + 20.0, 100.0 + 60.0, 200.0 + 150.0 and 350.0 + 275.0 respectively. Insets (A) plots of Ip vs. amlodipine concentrations and (B) plot of Ip vs. hydrochlorothiazide concentrations.

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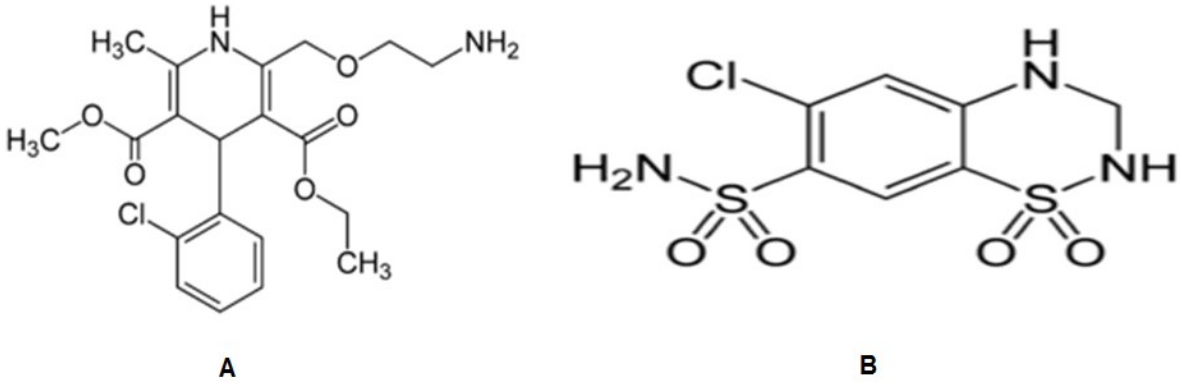

Scheme 1. Chemical structures of amlodipine (A) and hydrochlorothiazide (B).

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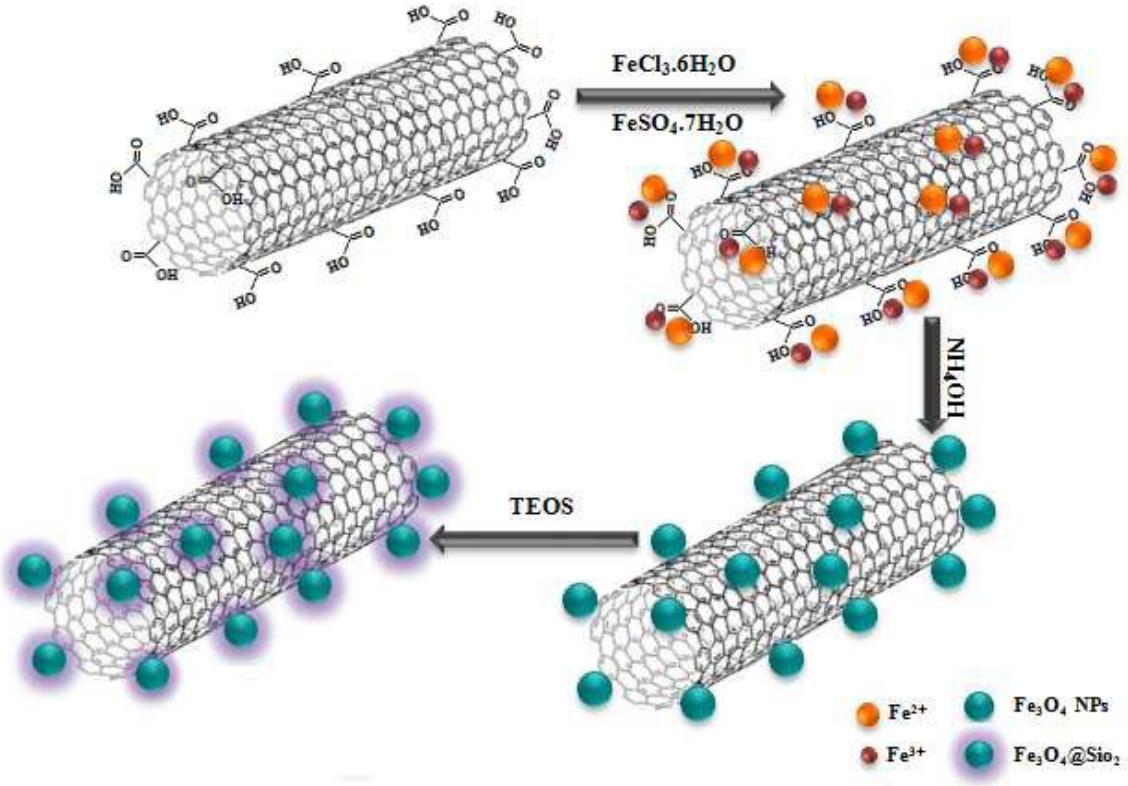

Scheme 2. Schematic representation of the preparation process of Fe_3O_4@SiO_2/MWCNT nanocomposite.

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Table 1 Comparison of oxidation of amlodipin and hydrochlorothiazide on various electrodes surface at pH 7.0.

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Electrode	Amlodipin		Hydrochlorothiazide	
	Anodic peak potential (mV)	Anodic peak current (μA)	Anodic peak potential (mV)	Anodic peak current (μA)
CPE	810	3.3	910	3.6
FSCNPE	780	5.5	880	6.2
ILCPE	730	15.5	840	12.1
ILFSCNPE	730	20.8	840	16.1

Table 2. Comparison of the efficiency of some modified electrodes used in the determination of amlodipine and hydrochlorothiazide.

Electrode	Modifier	Analyte	method	LOD (M)	LDR (M)	Ref.
Cathodically pretreated boron-doped diamond electrode	-	Amlodipine	Voltammetry	6.0×10^{-9}	2.0×10^{-7}–9.09×10^{-6}	3
		Hydrochlorothiazide		2.0×10^{-6}	4.0×10^{-6}–1.0×10^{-4}	
Cathodically pretreated boron-doped diamond electrode	-	Amlodipine	Voltammetry	2.3×10^{-7}	4.9×10^{-7}- 7.2×10^{-6}	9
		Hydrochlorothiazide		7.5×10^{-7}	2.9×10^{-6}- 4.4×10^{-5}	
Nickel	Nickel hydroxide	Hydrochlorothiazide	Voltammetry	7.92×10^{-6}	1.39×10^{-5}-1.67×10^{-4}	11
Carbon paste	-	Amlodipine	Voltammetry	2.0×10^{-10}	9.9×10^{-9} - 1.4×10^{-7}	12
Carbon paste	Magnetic core–shell Fe_3O_4@SiO_2/MWCNT/ Ionic liquid	Amlodipine	Voltammetry	1.5×10^{-7}	2.5×10^{-7} - 5.0×10^{-4}	This Work
		Hydrochlorothiazide		8.5×10^{-8}	1.0×10^{-6} - 6.0×10^{-4}	

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Table 3. Determination of amlodipine in amlodipine tablet and urine samples. All the concentrations are in μM (n=5).

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
Amlodipine tablet	0	10.0	-	2.7
	2.5	12.7	101.6	3.3
	7.5	17.1	97.7	2.3
	10.0	20.7	103.5	1.9
	12.5	22.3	99.1	2.7
Urine	0	ND	-	-
	10.0	9.7	97.0	3.6
	15.0	15.2	101.3	3.1
	20.0	20.4	102.0	2.2
	25.0	24.7	98.8	1.8

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Table 4. Determination of hydrochlorothiazide in hydrochlorothiazide tablet and urine samples. All the concentrations are in μM (n=5).

Sample	Spiked	Found	Recovery (%)	R.S.D. (%)
hydrochlorothiazide tablet	0	12.0	-	2.3
	5.0	17.5	102.9	3.5
	10.0	21.8	99.1	2.7
	20.0	32.5	101.6	2.9
	30.0	41.1	97.8	1.8
Urine	0	ND	-	-
	7.5	7.4	98.7	3.1
	12.5	12.7	101.6	2.2
	17.5	18.1	103.4	1.6
	22.5	22.3	99.1	2.3

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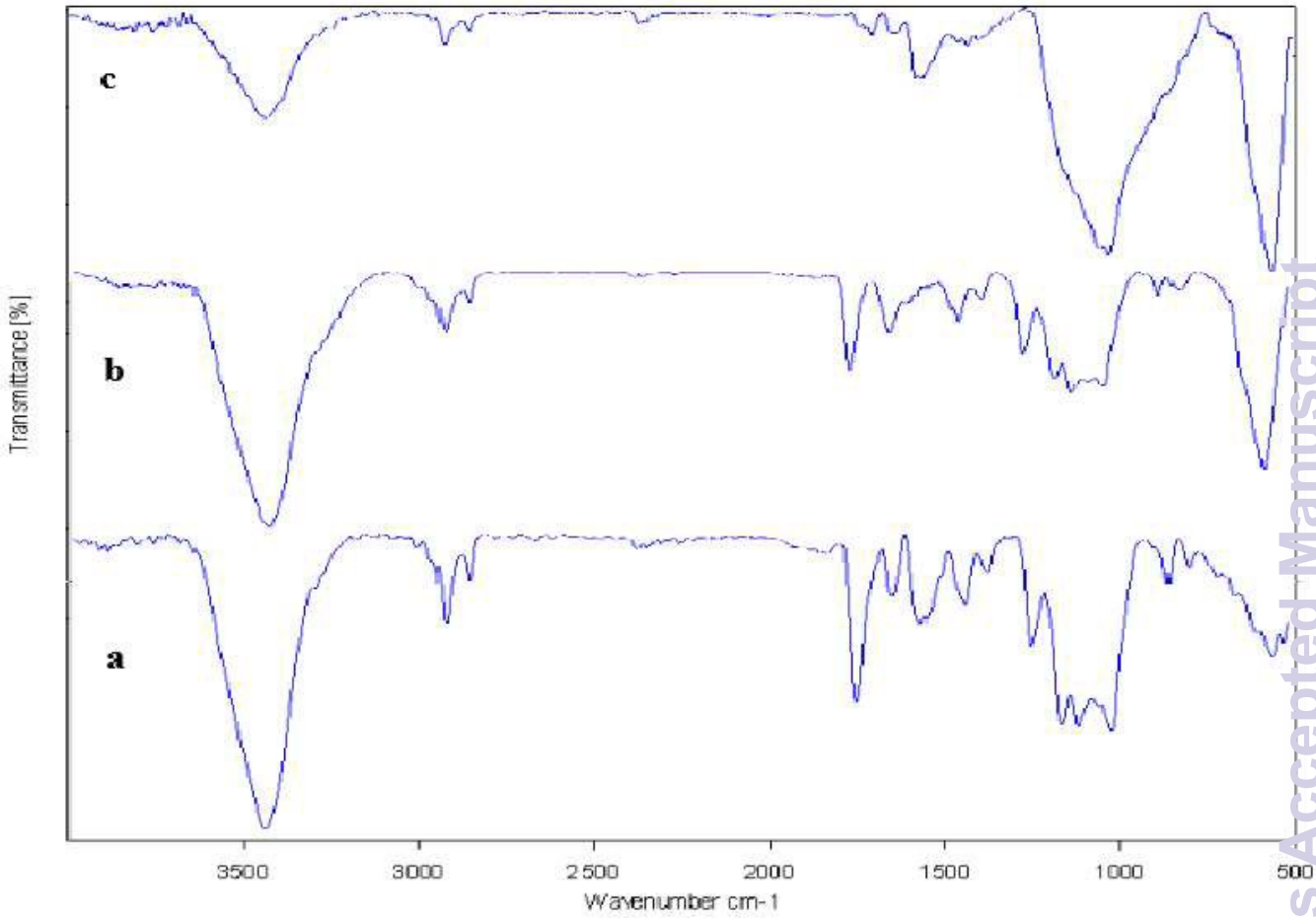

Fig. 1

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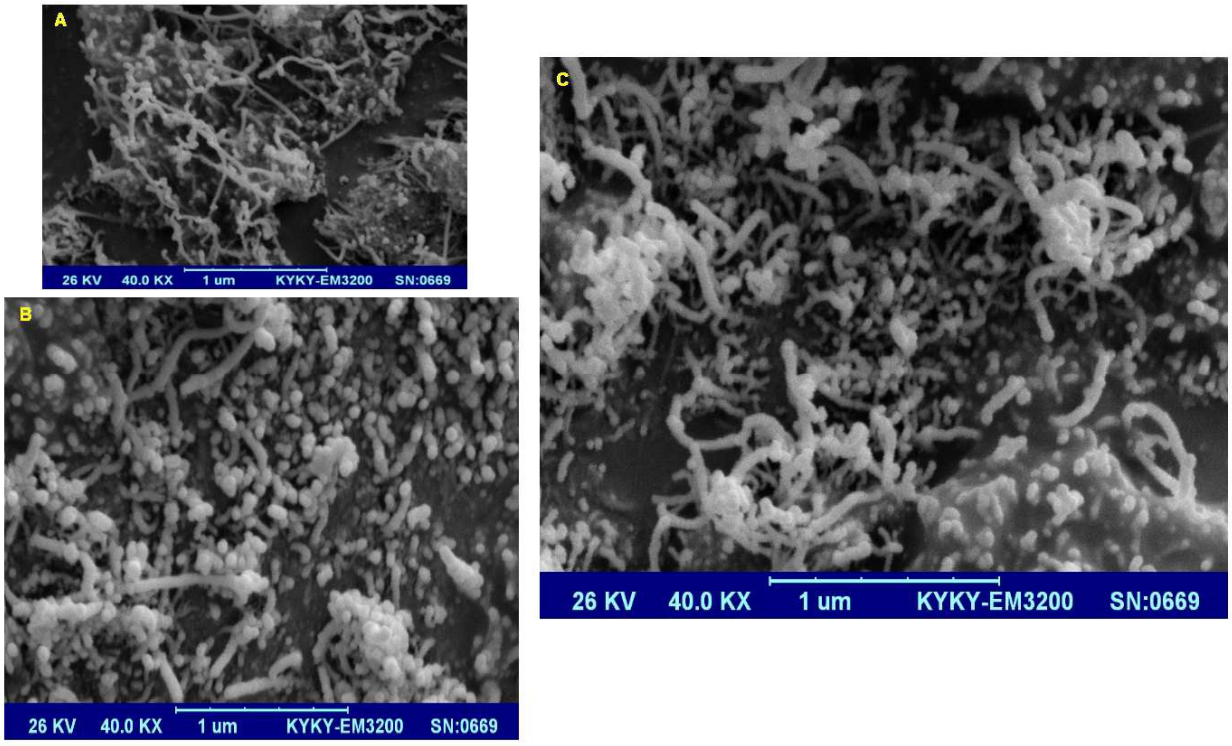

Fig. 2

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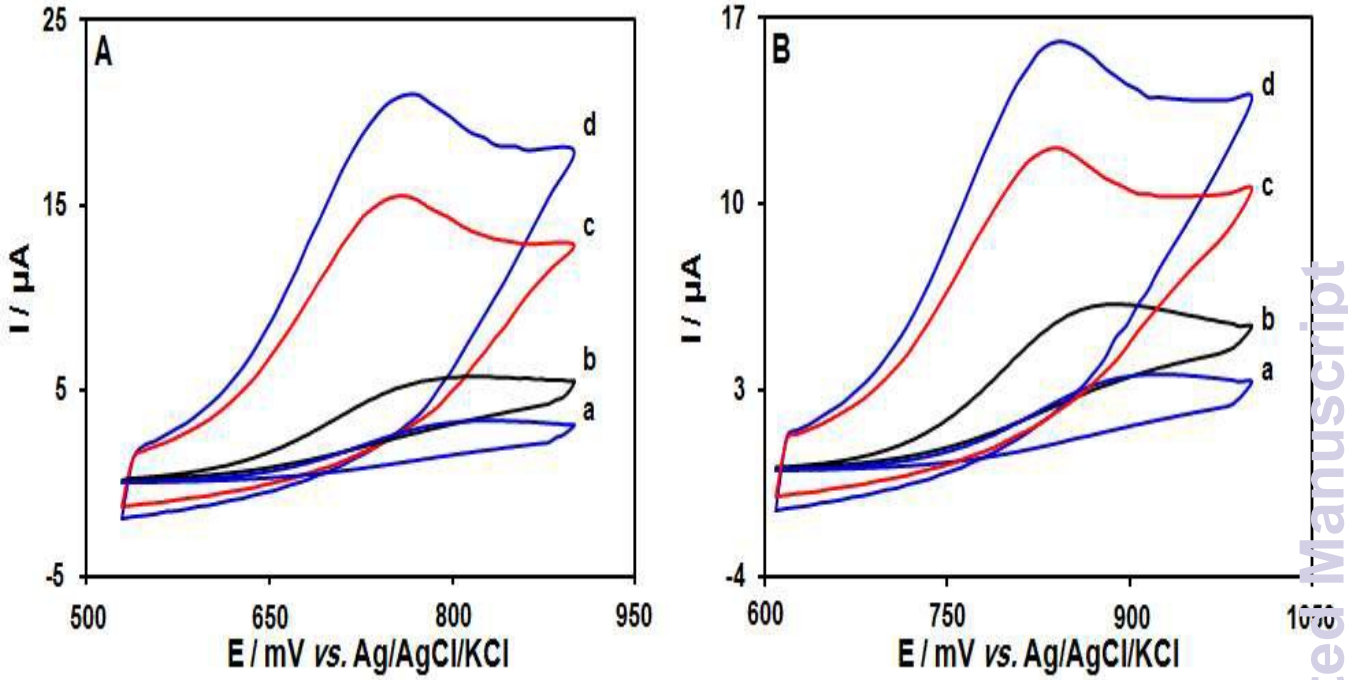

Fig. 3

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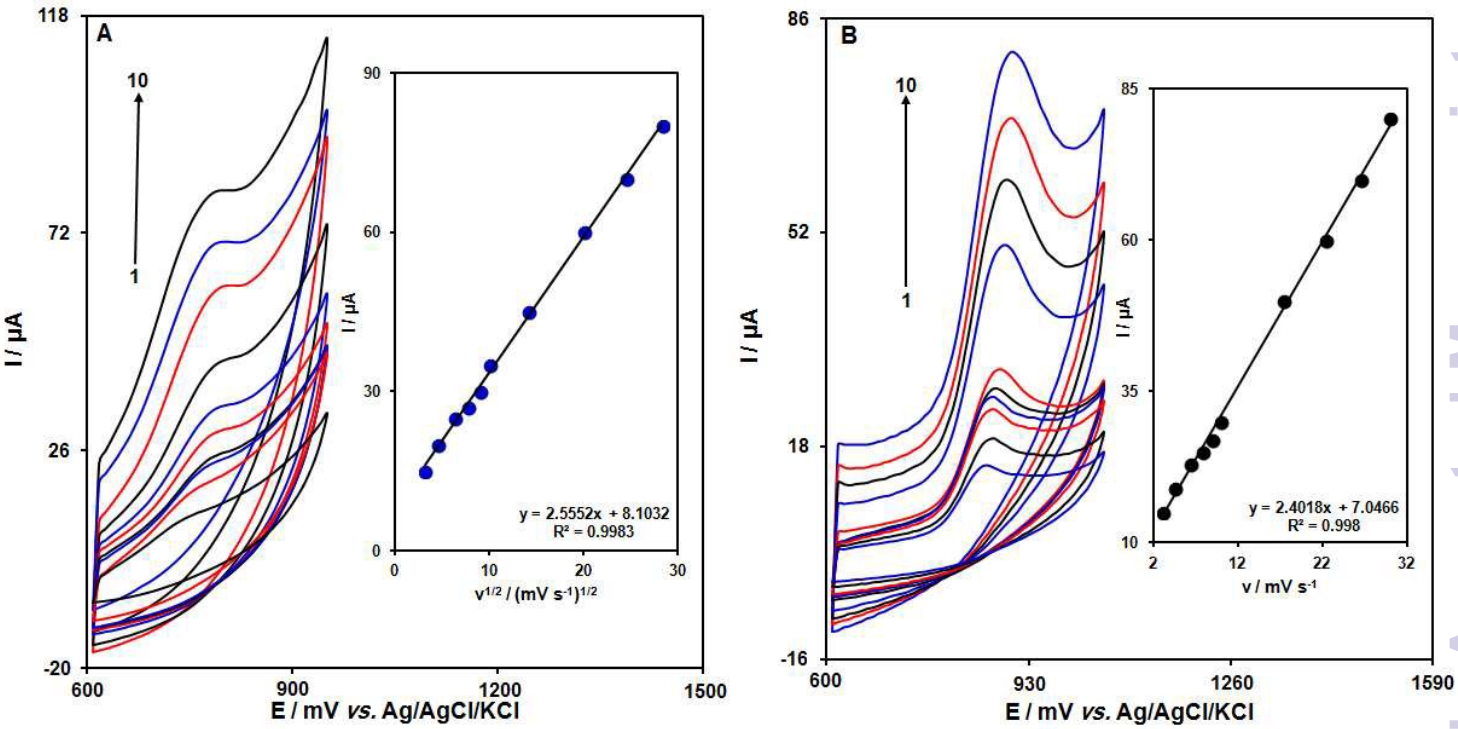

Fig. 4

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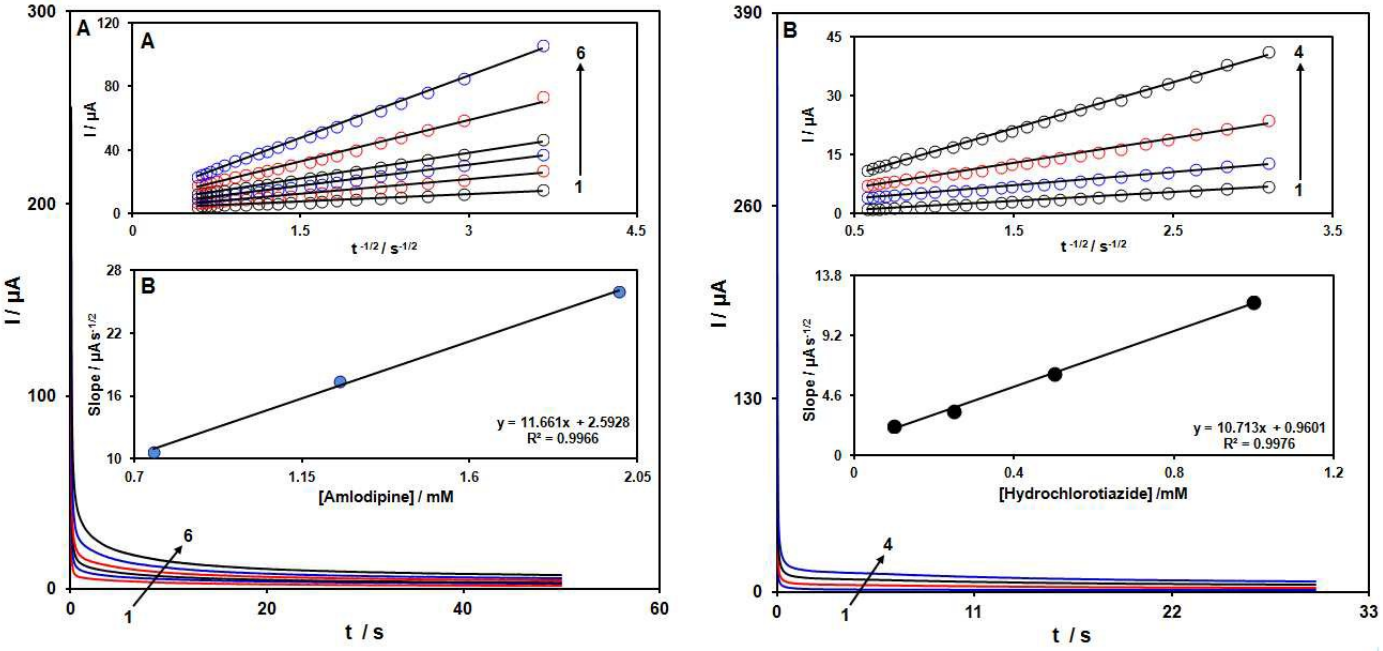

Fig. 5

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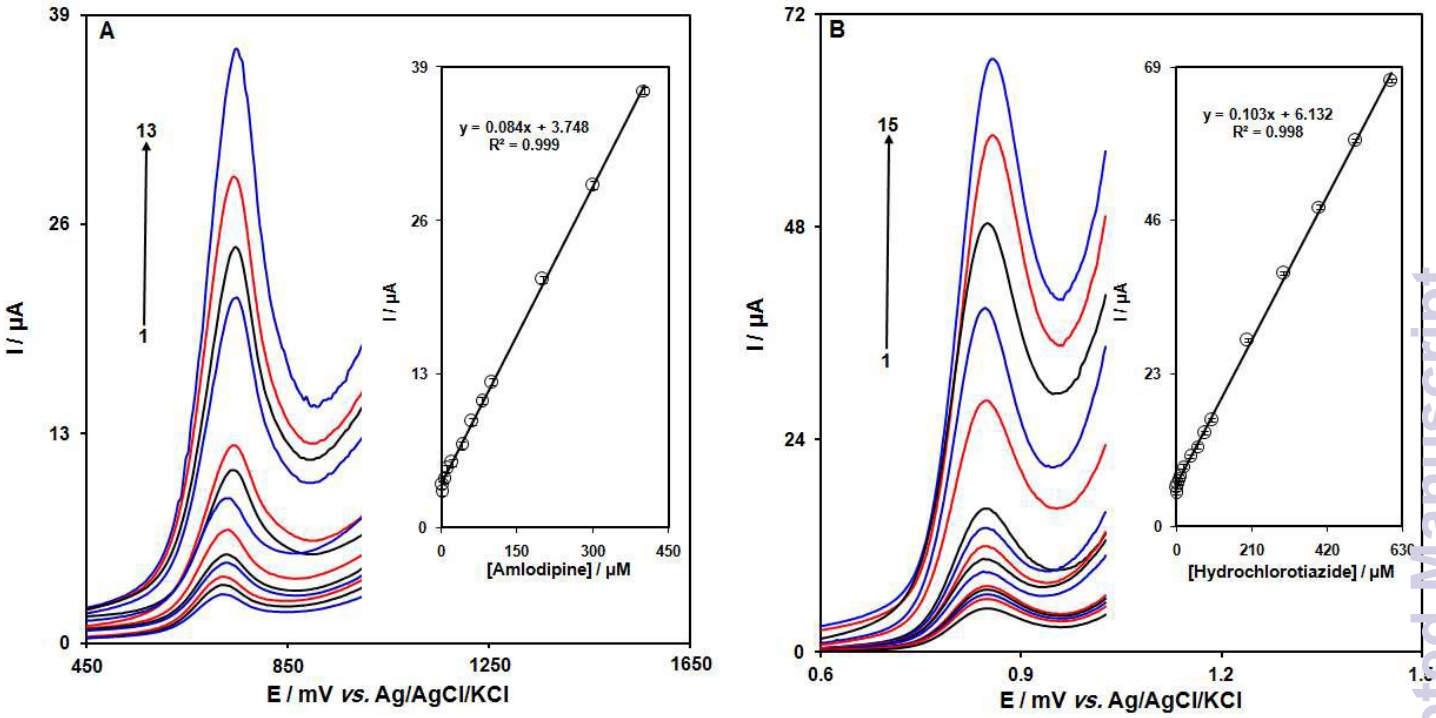

Fig. 6

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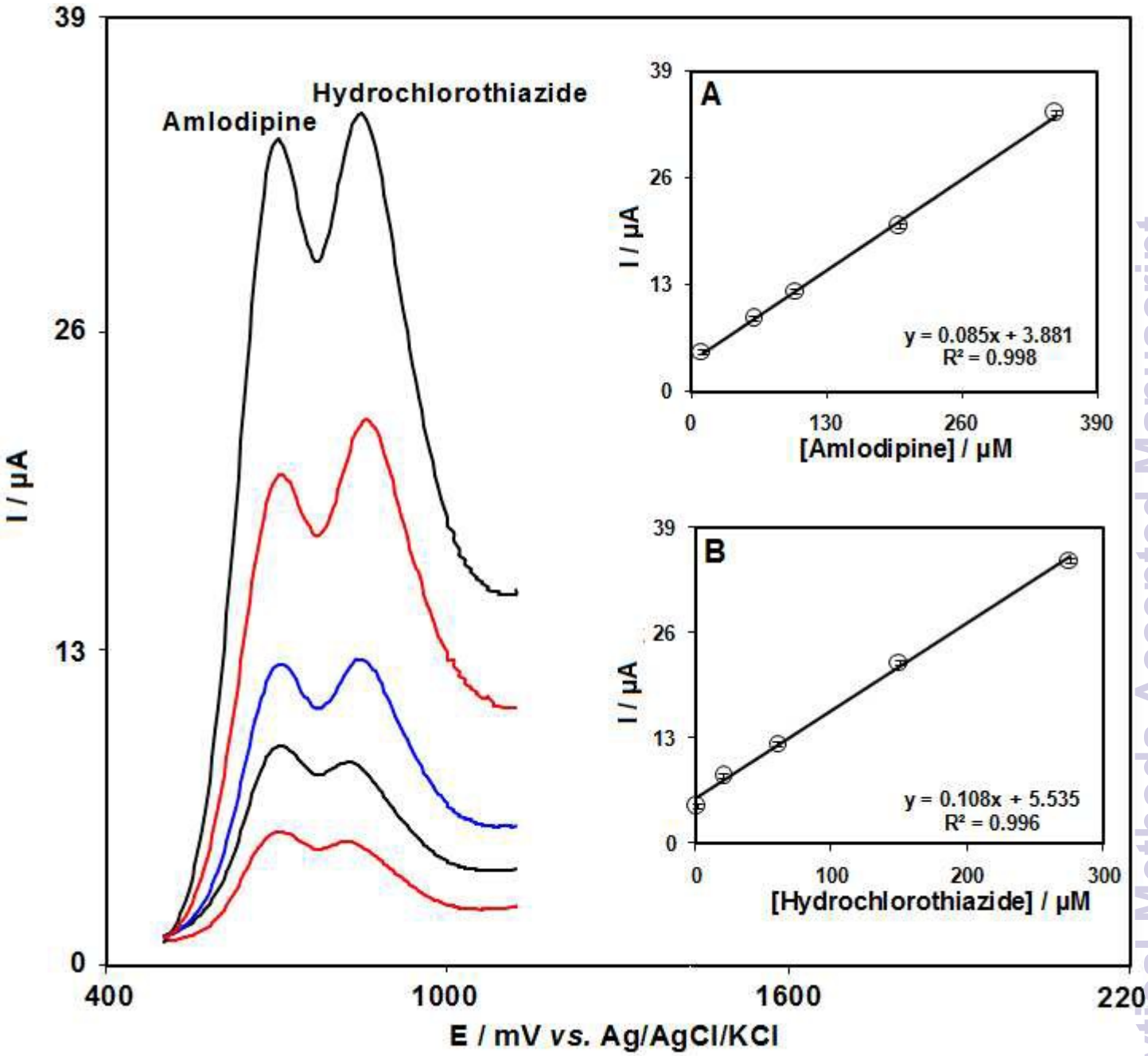

Fig. 7

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Magnetic core–shell Fe_3O_4@SiO_2/MWCNT nanocomposite modified carbon paste electrode for amplified electrochemical sensing of amlodipine and hydrochlorothiazide

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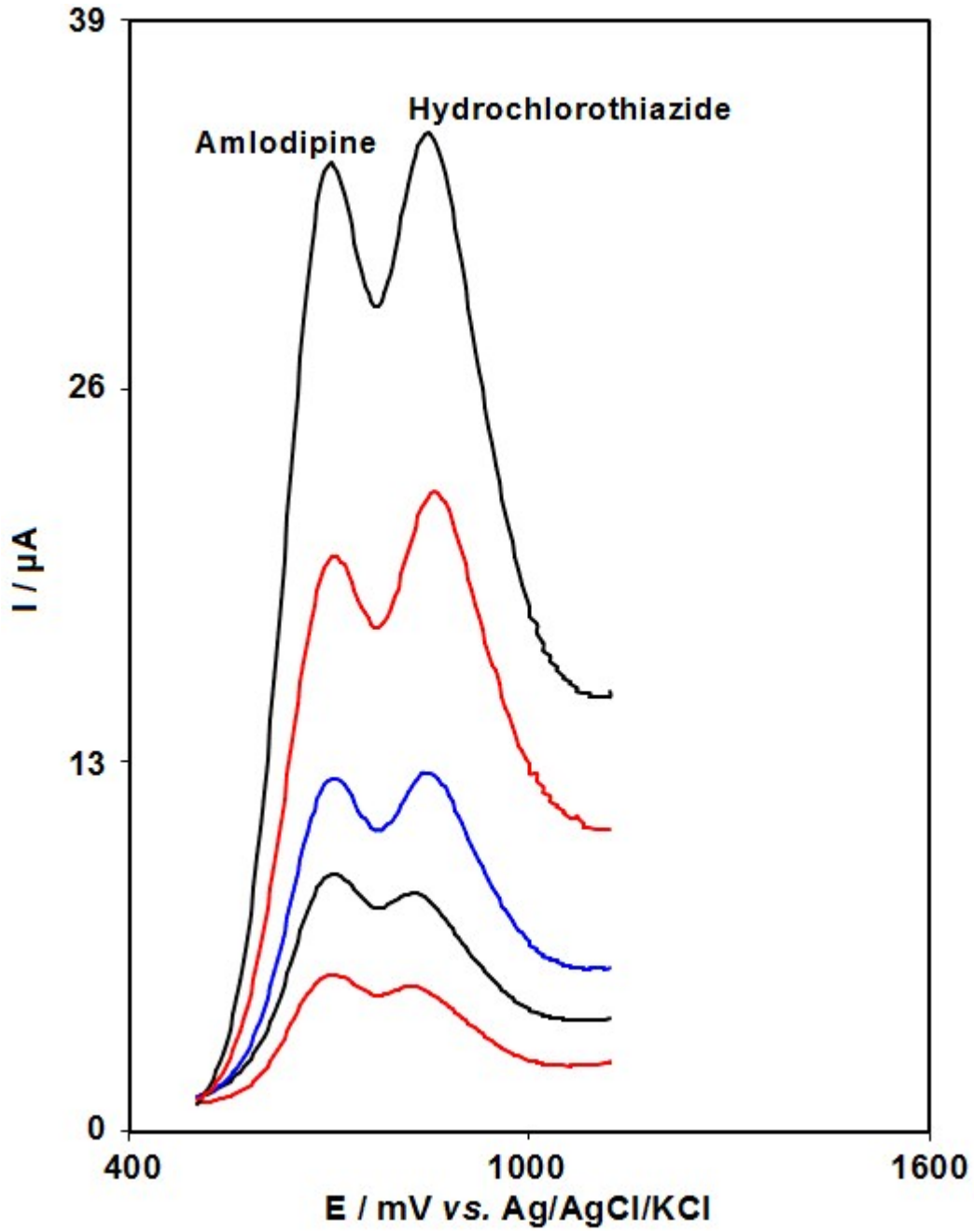

A novel carbon paste electrode for simultaneous determination of amlodipine and hydrochlorothiazid is constructed.