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Characterization and electrochemical investigations of micellar/drug interactions

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ABSTRACT

The effect of adding surface-active agents to electrolytes containing isoniazid (INH), an antituberculous drug, on the voltammetric response of carbon paste electrode (CPE) was studied. The enhancement of current signal due to the oxidation process was a function of the amount of analyte, pH of the medium, surfactants' type, and chain length and aromaticity and accumulation time at the electrode surface. Eight surfactants were used, three anionic type, sodium dodecyl sulphate (SDS), sodium octyl sulphate (SOS) and sodium dodecyl benzene sulphonate (SDBS), three cationic type, cetyl trimethyl ammonium bromide (CTAB), trimethyl octyl ammonium bromide (TMOB) and cetyl pyridinium bromide (CPB) and two nonionic surfactants, albumin and Triton X-405. Addition of SDS and SDBS to the isoniazid-containing electrolyte was found to enhance the oxidation current signals while SOS showed an opposite effect. The addition of either the cationic or nonionic surfactants was found to decrease oxidation current signals. To confirm the interactions between surfactant and isoniazid, absorbance spectroscopy has been performed. NMR measurements gave a good expectation for the location and orientation of INH in different micelles and gave a similar conclusion to that obtained from electrochemical and UV–vis data. The use of SDS in the electrochemical determination of isoniazid using differential pulse voltammetry at carbon paste electrode improved the limit of detection to 6.29 ng mL^{-1}. The validity of using this method in the determination of drug active ingredient in tablet formulations was also demonstrated.

1. Introduction

Surfactants have been widely used in chemistry and in particular affecting several electrochemical processes [1]. Several applications of surfactants in electrochemistry are in electroplating [2], corrosion [3], fuel cells [4], electrocatalysis [5], and electroanalysis [6]. The area of surface modified electrodes is of particular interest because of its application in sensors. Rusling [7] indicated the influence of surfactant aggregates at the electrode/electrolyte interface in micelle solutions. In his study [7], it was shown that the entry of an electrochemical reactant into this dynamic surface film is a key preceding electron transfer step. On the other hand, surfactants have proven effective in the electroanalysis of biological compounds and drugs. For example, it was recently shown that surfactants are highly effective in stabilizing the voltammetric response of serotonin by protecting the electrode surface from fouling [8]. In another study [9], it was shown that anionic surfactants could also be used to improve the accumulation of some electroactive organic molecules such as ethopropazine at gold electrodes. Recently, the influence of micelles in the simultaneous determination of two components was also demonstrated, as in the case of ascorbic acid and dopamine [10] and catechol and hydroquinone [11]. It was not clear whether the micelle interaction with the analyte in the solution phase contributes to the selective response. It is well established that interaction between aggregates and solutes in the solution phase is controlled by diffusion and takes place in the microsecond time scale [12]. Electrode surfaces with hydrophobic characters such as carbon paste electrodes interact with surfactants, namely through surface adsorption. Thus, carbon paste electrode modified with surfactants proved to be useful for the determination of both inorganic species [13] and biological compounds [14].

Drug analysis is an important branch of chemistry which plays an important role in drug quality control. Therefore, the development of sensitive, simple, rapid and reliable method for the determination of active ingredient is very important. Isoniazid or INH is a first-line antituberculous medication used in the prevention and treatment of tuberculosis. The structure of isoniazid is presented in Scheme 1.

Many analytical methods have been reported for the analysis of isoniazid, such as spectrophotometry [15–17], high performance liquid chromatography [18–21], capillary electrophoresis

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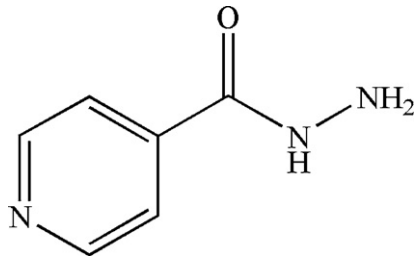

Scheme 1.

[22], chemiluminescence [23,24] and fluorimetry [25]. Several electrochemical methods have also been studied, such as differential pulse voltammetry at the gold electrode [26], squarewave adsorptive cathodic stripping voltammetry at the hanging mercury drop electrode [27], determination of isoniazid in urine using screen printed carbon electrode [28], cyclic voltammetry at the polypyrrole modified glassy carbon electrode [29,30] and the electrochemical oxidation of both the rifampicin (RIF) and isoniazid (INH) drugs by cyclic and square-wave voltammetry at a carbon paste electrode [31]. Determination of isoniazid using gold and silver nanoparticles has also been studied [32,33].

Up to date only few works were made on isoniazid using surfactants and techniques as HPLC and cloud point extraction [34] and flow-injection stopped-flow kinetic spectrophotometric method [35]. It is therefore essential to study the effect of changing the charge, chain length and aromaticity of the surfactants used its connection with the solution pH, and concentration of analyte on the voltammetric response of this drug. Moreover, in this work we relate the observed UV–vis and NMR measurements of isoniazid in the absence and presence of each surfactant type to the electrochemical data obtained.

2. Experimental

2.1. Materials and reagents

2.1.1. Metal substrates and electrochemical cell

A carbon paste (CP) electrode (3.0 mm diameter) from BAS (USA) was used as the working electrode, a platinum wire (2.0 mm diameter, 10 cm long) as auxiliary electrode, and an Ag/AgCl (3 mol L^{-1} NaCl) as the reference electrode. A one compartment glass cell (30 mL) fitted with gas bubbler was used for electrochemical measurements. Solutions were degassed using pure nitrogen prior to and throughout the electrochemical measurements.

2.1.2. Reagents and solution preparations

Isoniazid (INH) and Isocid® tablets (100 mg INH per tablet) were supplied by Novartis Pharma (Egypt). A stock solution of 1×10^{-2} mol L^{-1} INH was prepared with deionized water, freshly just prior to use. Britton–Robinson (B–R) buffer ($CH_3COOH + H_3BO_3 + H_3PO_4$), 4.0×10^{-2} mol L^{-1} of pH 2–11 was used as the supporting electrolyte. All solutions were prepared from analytical grade chemicals and sterilized Milli-Q deionized water. The anionic surfactants, sodium dodecyl sulphate (SDS) from Aldrich (USA), sodium octyl sulphate (SOS) from Fluka (USA), and sodium dodecyl benzene sulphonate (SDBS) from Fluka (Italy), the cationic surfactants, trimethyl octyl ammonium bromide (TMOB) from Fluka (Japan), cetytrimethyl ammonium bromide (CTAB) from Acros organics (New Jersey, USA, Geel, Belgium), and cetyl pyridinium bromide (CPB) from Prolabo (France), and the nonionic surfactants, albumin bovine from Mp Biomedicals (Germany), and Triton X-405 from Mp Biomedicals (France) were prepared as a stock solution of 0.01 M using deionized water and ultrasonicated for 30 min.

2.2. Electrochemical and spectroscopy instrumentations

The voltammetric measurements were performed using a PC-controlled AEW2 electrochemistry work station and data were analyzed with ECprog3 electrochemistry software (Sycopel, UK). The one-compartment cell with the three electrodes was connected to the electrochemical workstation through a C_3-stand from BAS (USA). A JENWAY 3510 pH meter (England) with a glass combination electrode was used for pH measurements. All UV measurements were performed using a Shimadzu 1601 spectrophotometer (Kyoto, Japan). NMR measurements were performed using a 300 MHz Varian NMR instrument in D_2O and with TEMAC as internal standard.

3. Results and discussion

3.1. Electrochemistry of isoniazid on carbon paste electrode

Fig. 1 compares typical cyclic voltammograms of 5×10^{-4} mol L^{-1} (INH) on bare CPE (in B–R buffer, pH 2.0) with scan rate 100 mV s^{-1} recorded using three different types of surfactants (i.e. anionic, cationic and neutral surfactant). INH on bare CPE without using any surfactant (solid line) exhibits a well defined irreversible oxidation peak at nearly +970 mV. The mechanism of anodic oxidation of isoniazid at the carbon paste electrode in aqueous media is expected to show a single two-electrons well-defined irreversible anodic peak, which may be attributed to oxidation of the amide moiety of isoniazid molecule [31]. Upon the addition of one of the anionic surfactants (SDS) (the dashed line) the anodic current response was increased and the anodic peak potential was shifted to a lower potential. While upon the addition of the cationic and the neutral surfactants CTAB and albumin respectively, the anodic current responses were decreased and the anodic peak potentials were shifted to higher potentials. This indicates the influence of using different types of surfactants on INH oxidation.

3.2. Electrochemistry of isoniazid on carbon paste electrode in situ modified with surfactant

The differential pulse voltammetry response of 5×10^{-4} mol L^{-1} INH (in B–R buffer, pH 2.0) on CPE upon five successive additions of each of the following surfactants: (SDS), (SDBS), (SOS), (CTAB),

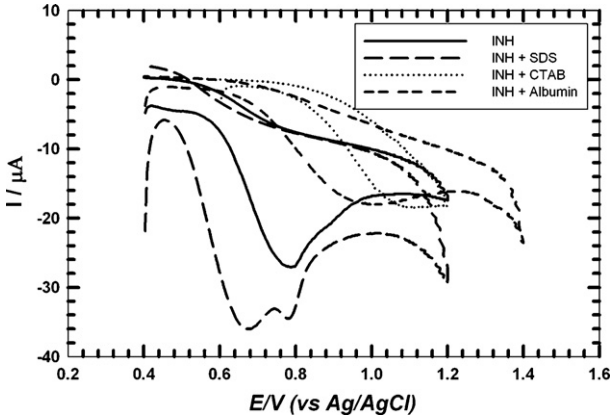

Fig. 1. Cyclic voltammograms of 5×10^{-4} mol L^{-1} (INH) on bare CPE (—) (in B–R buffer, pH 2.0) with scan rate 100 mV s^{-1}, using three different types of surfactants (i.e. SDS (– – –), CTAB (- - -) and albumin (. . .)).

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(TMOB), (CPB) Triton X-405 and albumin (increments added are 5 μl of 1×10^{-2} M surfactant) were studied. The suggested mechanisms for the aggregation of surfactants on the electrode surface in the form of bilayers, cylinders, or surface micelles (in the case of relatively higher concentrations added of surfactant) could explain the increase in current in the presence of surfactants [7]. The electron transfer process will take place when the electroactive species approaches the vicinity of the electrode surface. Two main possibilities allow the transfer of charge; first is the displacement of the adsorbed surfactant by the analyte, and second is the approach of the analyte to the surface of the electrode within the space of one to two head groups of adsorbed surfactant moieties. Furthermore, a possible mechanism suggests the formation of ion-pair that anchor onto the surface of the electrode that should posses some hydrophobic character [13].

INH is considered as a positively charged species especially at low pH values. Fig. 2A shows the oxidation peak current of INH before and after the addition of incremental additions of SDS. It is clear that the oxidation peak current of INH increased, since the electron transfer of INH was enhanced. Electrostatic attraction force between the positively charged drug INH and the negatively charged adsorbed surfactant film, as well as the hydrophobic interaction will act in a parallel way for the pre-concentration of INH on or into the adsorbed SDS and SDBS film. On the other hand, the oxidation peak current of INH decreased with incremental additions of SOS, this may be attributed to the difference in the structure of the surfactants, the short chain length of SOS that contains eight carbon atoms compared to SDS which contains 12 carbon atoms and SDBS which contains also 12 carbon atoms beside its aromatic ring. Fig. 2B shows the effect of the cationic surfactants CTAB on the oxidation peak current of INH, where the oxidation peak current of INH decreased with incremental additions, i.e. the electron transfer of INH will be inhibited. This effect may originate from the electrostatic repulsion between positively charged adsorbed film of surfactant and the positively charged INH. Finally, Fig. 2C shows how the oxidation peak current of INH decreases with incremental additions of the non-ionic surfactants (NIS) Triton X-405, this may reflect a lowering of the diffusion rate, considering the fact that the electroactive species exists away from the surface. The electrochemical oxidation mechanism of isoniazid is given in supplementary 1.

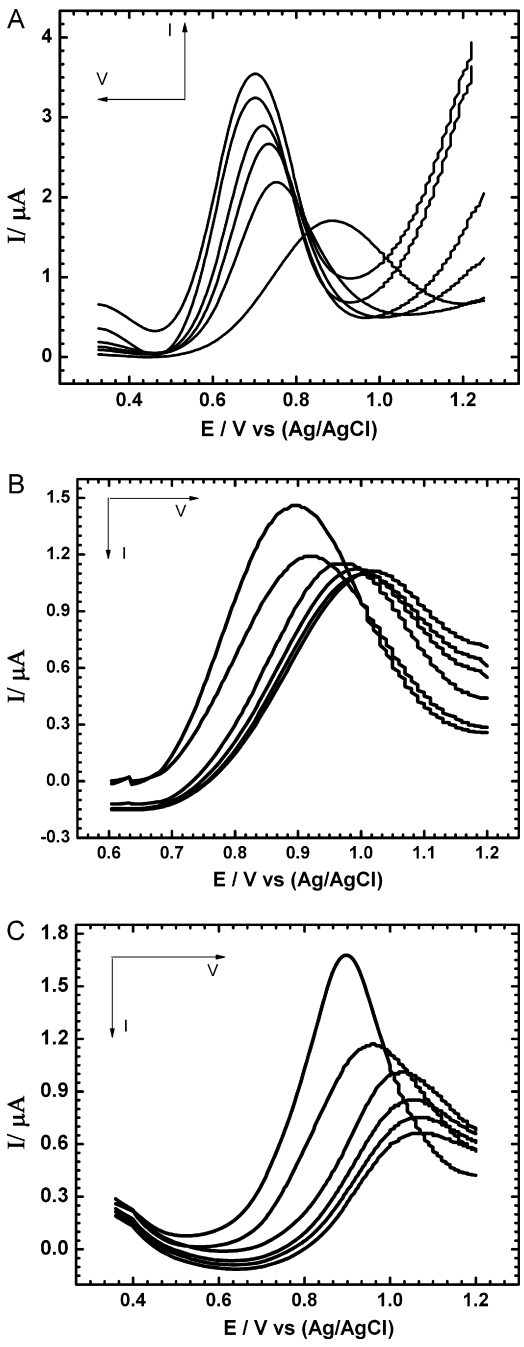

Fig. 2. (A) Effect of successive additions of SDS (increments added are 2.0×10^{-5} mol L^{-1} of each addition) on the voltammetric response of (INH) at pH 2 at carbon paste electrode, using differential pulse technique, scan rate 10 mV s^{-1}. (B) Effect of successive additions of CTAB (increments added are 2.0×10^{-5} mol L^{-1} of each addition) on the voltammetric response of (INH) at pH 2 at carbon paste electrode, using differential pulse mode, scan rate 10 mV s^{-1}. (C) Effect of successive additions of Triton X-405 (increments added are 2.0×10^{-5} mol L^{-1} of each addition) on the voltammetric response of (INH) at pH 2 at carbon paste electrode, using differential pulse technique scan rate 10 mV s^{-1}.

3.3. *Effect of pH on the electrochemical response of isoniazid in the absence and presence of surfactant*

INH can be considered lipophilic in nature with a reported pK_a values of 1.8 based on hydrazine nitrogen, 3.5 based on pyridine nitrogen and 10.8 based on acidic group [36]. Fig. 3A–C shows a comparison between the anodic peak currents in the presence and absence of SDS, SDBS, SOS, CTAB, TMOB, CPB, Triton X-405 and albumin respectively over a wide range of pH values (2.0 → 9.0). The presence of the anionic surfactants, SDS and SDBS results in a shift in the anodic peak potential to less positive values especially at low pH values, while SOS has an opposite trend (not shown), indicating that protons are directly involved in the oxidation of INH. At low pH values INH could be considered as a positively charged species [37]. Thus, the chance for the electrostatic interaction between the positively charged drug and the negatively adsorbed surfactant film will be enhanced. As a result, the oxidation process will be facilitated and will occur at lower potentials. On the other hand, maximum oxidation current signal occurred at pH 2.0 in the SDS and at pH 5.0 in SDBS and SOS-containing solutions. As can be seen from Fig. 3A, the adsorbed anionic surfactant film promoted the pre-concentration of isoniazid on the electrode surface especially at low pH values. While upon the addition of the cationic surfactants (Fig. 3B), the oxidation peak current of INH always decrease but with different values, i.e. the decrease in the anodic peak current of INH in the presence of CTAB and CPB are more than in case of TMOB especially at pH 5.0. For the non-ionic surfactants Triton X-405 or albumin, Fig. 3C shows that the oxidation peak current of INH decreases for the whole pH range, but there is only a small increase in the current response in case of Triton X-405 compared to albumin at pH 5.0. The pH dependency of the oxidation peak potential indicates that protonation/deprotonation is taking part in

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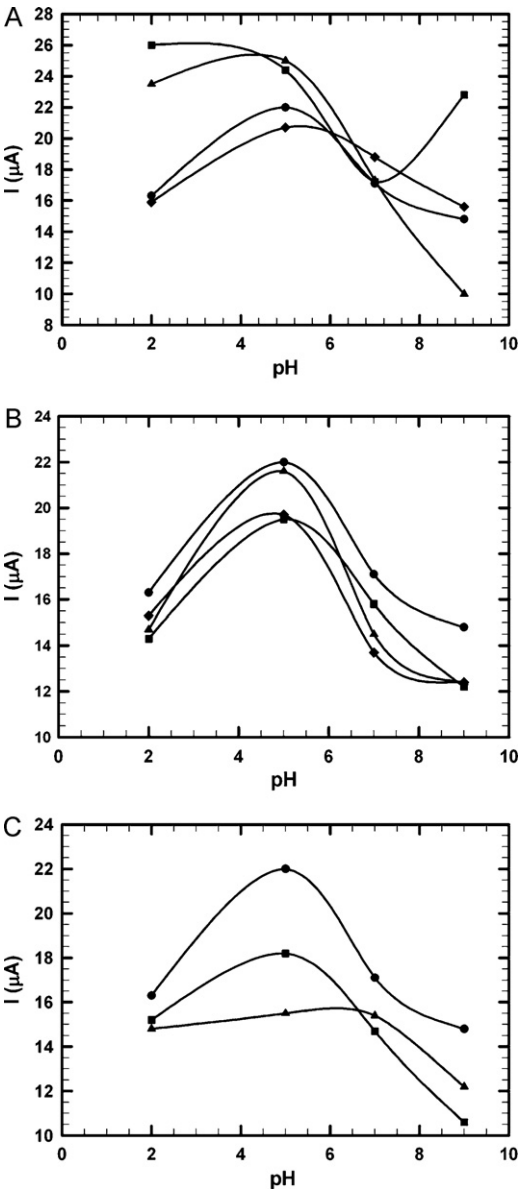

Fig. 3. (A) Effect of pH on the oxidation peak current of INH (5×10^{-4} M) in absence (●) and in presence of SDS (■), SDBS (▲) and SOS (♦) (10^{-4} M). (B) Effect of pH on the oxidation peak current of INH (5×10^{-4} M) in absence (●) and in presence of CTAB (■), TMOB (▲) and CPB (♦) (10^{-4} M). (C) Effect of pH on the oxidation peak current of INH (5×10^{-4} mol L^{-1}) in absence (●) and presence of Triton X-405 (■), albumin (▲) (10^{-4} mol L^{-1}).

the charge transfer process. Also the study showed that the difference in the structure of surfactants gave different interactions with INH in the studied pH range. There is a possibility of ion-pairing that could be incomplete in this case. For instance, the charged isoniazid methanesulfonate could be ion paired with hydrophobic cations, such as alkyltrimethylammonium or tetraalkylammonium [38].

3.4. Effect of scan rate on the voltammetric response of isoniazid

The relation between anodic peak current, i_{pa} (μA), diffusion coefficient of the electroactive species, D_0 ($cm^2\ s^{-1}$), and scan rate, ν ($mV\ s^{-1}$), is given by Randles–Sevcik equation:

$$i_{pa} = (2.69 \times 10^5) n^{3/2} \alpha A C_0 \times D_0^{1/2} \nu^{1/2} \quad (1)$$

where n is the number of electrons exchanged in oxidation, α is the transfer coefficient, A is the apparent surface area of the electrode (cm^2), and $C_0{}^*$ is the concentration of the electroactive species (mol/cm^3). The transfer coefficient for an irreversible process can be calculated from:

$$\left|E_{pa} - E_{pa/2}\right| = \frac{47.7}{\alpha} \quad (2)$$

where $E_{pa/2}$ is the potential at which the current equals one half of the peak current [39]. A plot of i_{pa} versus $\nu^{1/2}$ (ν ranging from 10 to 250 $mV\ s^{-1}$) for SDS, SDBS, and SOS gave a straight line according to Eq. (1). This reveals that the linearity of the relationship is realized up to a scan rate of 100 $mV\ s^{-1}$ that is followed by a deviation from linearity with increasing scan rate. This indicates that the charge transfer is under diffusion control partially and that the adsorption of aggregates at the electrode surface is also possible. (D_0) can be calculated and are listed in Table 1. The size of the diffusion layer at the electrode surface proximity changes with the voltage scan used. At relatively slow voltage scans, the diffusion layer grows much further towards the solution side and further from the electrode surface. Therefore, as the scan rate increases, the flux to the electrode surface increases considerably. At relatively higher scan rates and in the presence of SDS, SDBS and SOS, the diffusion layer grows less further from the vicinity of the electrode. The values indicated in Table 1 for D_0 show that the diffusion is enhanced in the presence of SDS and SDBS and that the lowest value was in the presence of SOS, which is due to the different in the structure between the three anionic surfactants as was mentioned before. The values reported are relative and cannot be considered as absolute.

3.5. Effect of accumulation time on the electrochemical response of isoniazid

The effect of accumulation time on the anodic peak current of 5×10^{-4} mol L^{-1} INH was investigated in the presence of 1.0×10^{-4} mol L^{-1} SDS, SDBS, and SOS, in B–R buffer with different pH values, under open circuit. The reported pK_a values of INH as was mentioned before in Section 3.3 and changing the pH of the electrolyte was found to affect the electrochemical response of the drug in the presence of different anionic surfactants. Fig. 4A shows the effect of accumulation time on the anodic peak current of INH in the presence of SDS at different pH values. It is clear that the oxidation peak current of INH at pH 2.0 gives the highest response at 6 min, while at pH 9.0 the response disappeared after 4 min stirring which indicates the blocking of the surface by the surfactant molecules. In case of SDBS, Fig. 4B shows that INH at pH 2.0 gives the highest response but there is no obvious effect at pH 5.0 and pH 7.0 and there is no distinct response appeared at pH 9.0. Fig. 4C shows that in the presence of SOS the anodic peak current of INH at pH

Table 1
Electrochemical parameters of INH determined at carbon paste electrode in different electrolyte solutions using cyclic voltammetric technique.

Electrolyte B–R buffer, pH = 2	[a] E_{pa} (mV) (vs. Ag/Agcl)	[a] I_{pa} (μA)	α	D_0 ($cm^2\ s^{-1}$)
5×10^{-4} mol L^{-1} INH	970	16.3	0.25	5.994×10^{-8}
5×10^{-4} mol L^{-1} INH + 1×10^{-4} mol L^{-1} SDS	802	26.0	0.46	1.12×10^{-7}
5×10^{-4} mol L^{-1} INH + 1×10^{-4} mol L^{-1} SDBS	873	23.5	0.27	1.19×10^{-7}
5×10^{-4} mol L^{-1} INH + 1×10^{-4} mol L^{-1} SOS	960	15.2	0.26	5.11×10^{-8}

[a] Donate that both, E_{pa}, and I_{pa}, were determined at scan rate, $\nu = 100\ mV\ s^{-1}$.

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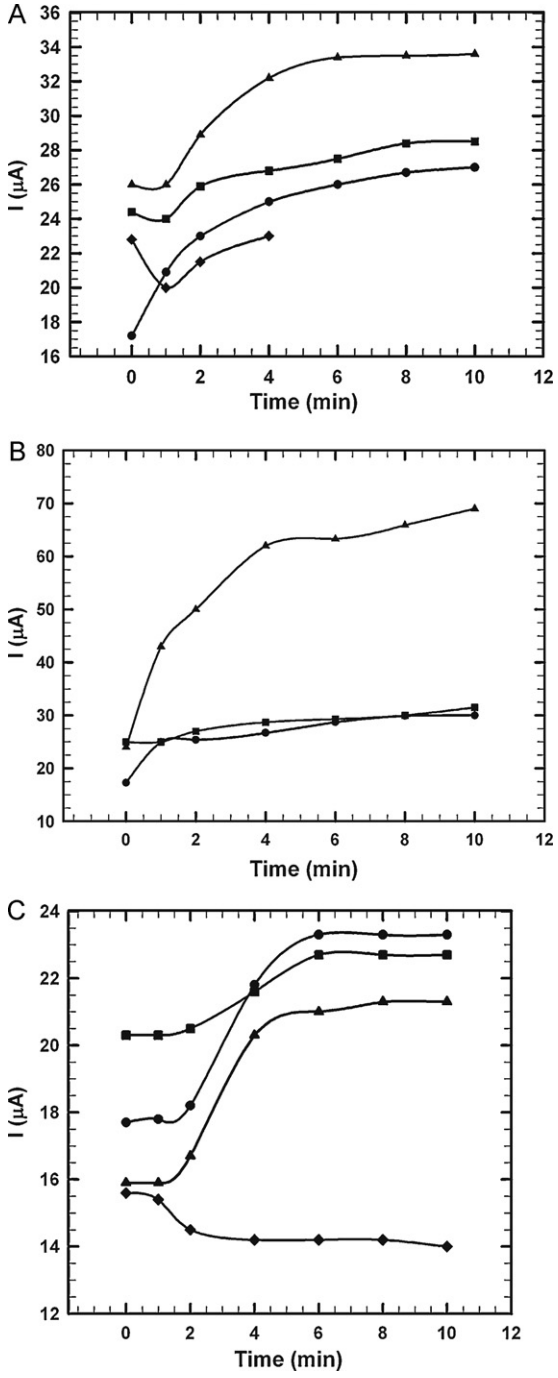

Fig. 4. (A) Effect of accumulation time on the oxidation peak current of INH (5×10^{-4} mol L^{-1}) in the presence of SDS (10^{-4} mol L^{-1}), (pH 2 (▲), pH 5 (■), pH 7 (●), pH 9 (♦)). (B) Effect of accumulation time on the oxidation peak current of INH (5×10^{-4} mol L^{-1}) in the presence of SDBS (10^{-4} M), (pH 2 (▲), pH 5 (■), pH 7 (●), pH 9 (♦)). (C) Effect of accumulation time on the oxidation peak Current of INH (5×10^{-4} mol L^{-1}) in the presence of SOS (10^{-4} M), (pH 2 (▲), pH 5 (■), pH 7 (●), pH 9 (♦)).

2.0, 5.0 and 7.0 increased as the accumulation time increased then become steady constant after 6 min, at pH 7 the highest oxidation peak current was obtained, while at pH 9 there is a slight decrease in the oxidation peak current with increasing accumulation time. The change in the current response values in the presence of different surfactants at different pH values were due to two factors, the pH of the medium and the structure of the surfactants as was discussed before.

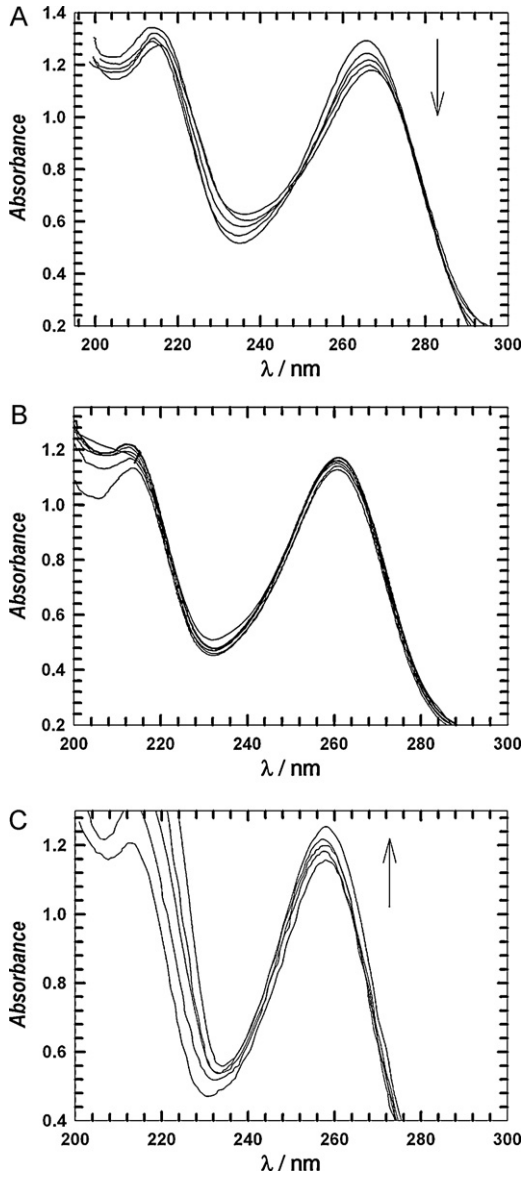

Fig. 5. (A) The effect of successive additions of SDS surfactant on the absorption spectrum of 2×10^{-3} mol L^{-1} INH (in B–R buffer, pH 2), each increment is 6×10^{-6} mol L^{-1}. (B) The effect of successive additions of CTAB surfactant on the absorption spectrum of 2×10^{-3} mol L^{-1} INH (in B–R buffer, pH 2), each increment is 4×10^{-5} mol L^{-1}. (C) The effect of successive additions of Triton X-405 surfactant on the absorption spectrum of 2×10^{-3} mol L^{-1} INH (in B–R buffer, pH 2), each increment is 4×10^{-5} mol L^{-1}.

3.6. UV–vis studies

Interactions of different types of surfactants with isoniazid in aqueous B–R buffer solutions were followed by UV–vis spectroscopy.

Fig. 5A shows the effect of successive additions of SDS surfactant on the absorption spectrum of 2×10^{-3} mol L^{-1} isoniazid at pH 2.0. Basically, the anionic surfactants SDS and SOS show no absorption background, while SDBS gives a peak at 269 nm (UV absorption of the aromatic group) which was removed by a blank. The anionic character of SDS and SDBS favors coulombic forces with the drug and should lead to the formation of aggregates in the solution phase.

The observations have been attributed to the formation of closely packed drug-surfactant ion-pair. Also, there is no red nor blue shifts taking place upon the addition of surfactants, the only change is the reduction of the absorption intensity. This indi-

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cates that the charge interaction of the drug with SDS and SDBS is the main contribution to the association that resulted in the decrease in the absorption spectra. SOS shows a different trend (not shown), since it causes the absorption intensity to decrease and then increase at all the pH values which may be due to its short chain length compared to SDS and SDBS.

The absorption intensity of the 266 nm band in absence, and presence of 2.4×10^{-5} M SDS, SDBS and SOS, at different pH values showed that, the absorbance decreases as the pH increases in the presence and/or in the absence of the surfactants, which indicates that protons are involved in the interaction between INH and surfactants on the electrode surface as was mentioned before.

On the other hand, the effect of successive increasing of the concentration of the cationic surfactants TMOB, CTAB, and CPB (each increment in the surfactant concentration = 4×10^{-5} mol L^{-1}), on the absorption spectrum of 2.0×10^{-3} mol L^{-1} INH, in B–R buffer of different pH values was studied. The only observed change is in the intensity of the peaks at the whole pH range. Columbic repulsion is expected to occur that should result in the exclusion of INH. Hence, these columbic repulsive forces between the positively charged INH and the positive ammonium group of TMOB and CTAB, and the positive nitrogen in the pyridine ring of CPB preventing the aggregation of the drug molecules with the cationic surfactant's micelles. Therefore, the only existing attractive forces competing with the repulsive ones are the hydrophobic interactions. Fig. 5B shows the effect of successive additions of CTAB on the absorption spectrum of 2×10^{-3} mol L^{-1} INH, at pH 2.0. The absorption intensity of INH decreases with increasing the pH, in presence and absence of the three cationic surfactants, it is also obvious that the increase in the absorption intensity of INH upon the successive additions of TMOB is less compared to CTAB that contains a longer chain length and CPB that contains a benzene ring (not shown).

Fig. 5C shows the data of the successive additions of Triton X-405 on the absorption spectrum of INH. The nonionic surfactants show a different trend from that of the anionic and the cationic surfactants, i.e. a bathochromic shift in the maximum absorption peak from 266 nm to 272 nm is obtained, which indicates the presence of an interaction between INH and these nonionic surfactants. In the presence of nonionic surfactants the absorbance increases with increasing the pH of the solution, then becomes nearly constant at pH value more than 5.0 this behavior may be due to the absence of an electrostatic effect so the polarity of the neutral surfactants is the dominant factor affect the dissociation equilibrium of INH, also the smaller polarity of Triton X-405 and albumin compared to that of water, decreases the dissociation of INH.

The spectrophotometry data are in good agreement with what we obtained in the voltammetry experiments. One important conclusion is that the aggregation of an electroactive species is still possible at submicellar concentrations depending on the strength of binding with the corresponding surfactant.

3.7. NMR studies

The H^1 NMR spectra of 0.001 mol L^{-1} of INH at pH 2.0 is given in Fig. 6A, there are two characteristic quartet signals of the amide and the aromatic pyridine moiety, from 9 PPM to 9.11 PPM and from 8.47 PPM to 8.5 PPM.

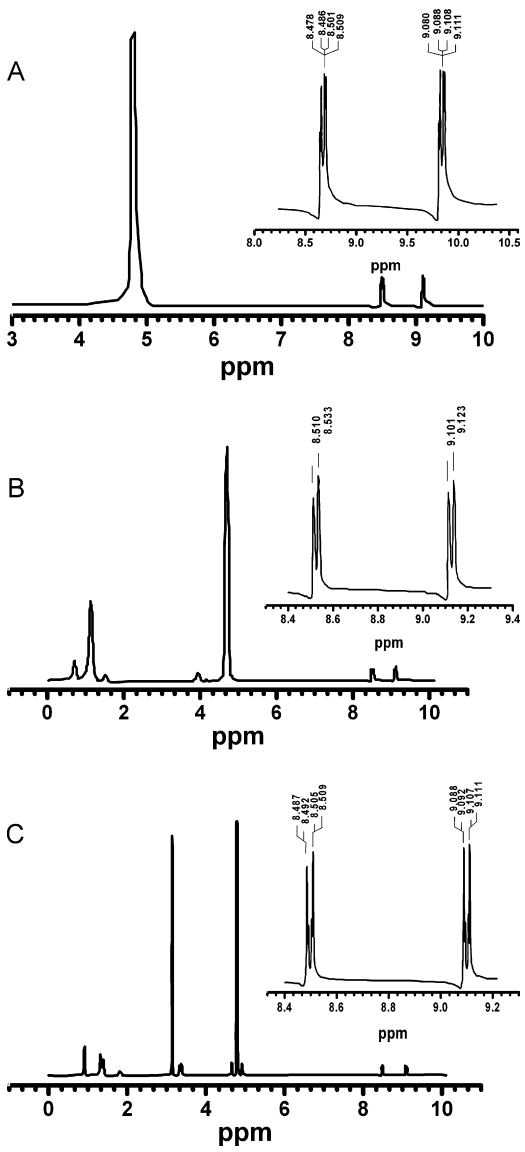

Fig. 6. (A) H^1 NMR spectrum of INH, (B) H^1 NMR spectrum of SDS mixed with INH and (C) H^1 NMR spectrum of TMOB mixed with INH.

Fig. 6B shows H^1 NMR spectra of 0.001 mol L^{-1} INH mixed with 0.01 mol L^{-1} SDS at pH 2.0, chemical shift changes for INH protons upon mixing with SDS show that the protons of the pyridine ring of INH undergoes a down-field chemical shift as shown in Table 2. We believe that, the most adjacent protons of INH to the electrostatic interaction center are the aromatic protons of the pyridine moiety, because of the inductive effect of the heteroatom nitrogen. It could be noticed that through the three figures, there is a common intense peak at nearly 4.80 PPM which is attributed to the D_2O solvent.

On the other hand, mixing INH with TMOB as shown in Fig. 6C causes a down-field chemical shift for INH protons. The values of the chemical shift are much smaller than in the case of SDS as

Table 2
NMR chemical shift of INH in D_2O and their variation ($\Delta\delta$) in presence of SDS.

Samples	Aromatic protons [Drug chemical shift, PPM]							
In absence of SDS	9.111	9.103	9.088	9.080	8.509	8.501	8.486	8.478
In presence of SDS	9.123	–	9.101	–	8.533	–	8.510	–
$\Delta\delta$[a]	0.012	–	0.013	–	0.024	–	0.024	–

[a] Means that ($\Delta\delta$) is the shift in presence of SDS subtracted from the shift in its absence.

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Table 3
NMR chemical shift of INH in D_2O and their variation ($\Delta\delta$) in presence of TMOB.

Samples	Aromatic protons [Drug chemical shift, PPM]							
In absence of TMOB	9.111	9.103	9.088	9.080	8.509	8.501	8.486	8.478
In presence of TMOB	9.111	9.107	9.092	9.088	8.509	8.505	8.492	8.487
$\Delta\delta$[a]	0	0.004	0.004	0.008	0	0.004	0.006	0.009

[a] Means that ($\Delta\delta$) is the shift in presence of TMOB subtracted from the shift in its absence.

shown in Table 3. This is due to the repulsive coulombic forces between the positively charged amino-group of INH and the positively charged head-group of TMOB, prevent the aggregation of the drug molecules in solution, and the only existing attractive forces competing with the repulsive ones are the hydrophobic interactions, however, it is still a minor action. From these results we find that the NMR data give a similar conclusion to that obtained from electrochemical or UV–vis data.

3.8. Application on commercial tablets

Under the optimized experimental conditions mentioned above, the relationship between the peak current and the concentration of INH was investigated., in the presence of 1.0×10^{-4} mol L^{-1} SDS at pH 2.0, using DPV mode, measured with CP working electrode and an accumulation time of 6 min. The parameters for the DPV experiments are: E_i = +300 mV, E_f = +1000 mV, scan rate = 10 mV s^{-1}, pulse width = 25 ms, pulse period = 200 ms, and pulse amplitude = 10 mV. As presented in Fig. 7 and its inset, the current response increased with the increase of INH concentration from 1.3 to 100 ng mL^{-1} with a correlation coefficient of 0.9991. The regression equation was i (μA) = 0.068 C (ng mL^{-1}) + 0.7927, where i is the current intensity, and C is the INH concentration. The detection limit LOD (3α, n = 12) is estimated to be 6.29 ng mL^{-1} and the limit of quantitation LOQ = 20.99 ng mL^{-1} calculated from the equation: LOD = 3 s/m and LOQ = 10 s/m [40], where s is the standard deviation (s = 0.143 ng mL^{-1}) and m is the slope of the calibration curve.

Accuracy and precision of the proposed method were determined by replicate analyses of five different concentrations of INH, the results were given as shown in Table 4. The recovery was found in the range from 98.0% to 101.4% and the relative standard deviation (RSD) was in the range from 0.35% to 0.93%.

The above procedure was also used for the determination of INH in commercial tablets; Isocid (100 mg/tablet INH) was analyzed without pre-measurement treatments. Isocid stock solution of concentration 1.0×10^{-2} mol L^{-1} was prepared as mentioned in the experimental part. An aliquot of this solution added (using a microsyringe) to a 5 ml (B–R buffer-pH 2.0 containing 1.0×10^{-4} mol L^{-1} SDS) and the DPV was recorded under the same conditions described above. Then, standard addition of 10 μL of INH standard stock solution was added and the corresponding DPV was measured. Table 5 shows the data generated by standard addition method for the analysis of Isocid in buffered solution of pH 2.0. The data represented are calculated from five replicates.

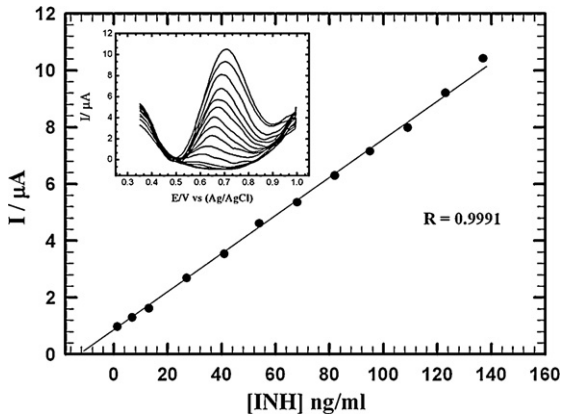

Fig. 7. Calibration curve of the oxidation peak currents of (i_{pa}), versus the concentration of INH (in B–R buffer, pH 2.0) using differential pulse technique. The inset represents the DPV of different concentrations of INH, in the presence of 1.0×10^{-4} mol L^{-1} SDS.

Table 4
Evaluation of the accuracy and precision of the proposed method for the determination of (INH).

Analytical parameters for the determination of INH	
Five different concentration of INH; number of replicates (n) = 5	
Parameter	DPV mode
Linearity range (ng/ml)	1.3–137
Calibration curve equation	i (μA) = 0.068 C (ng mL^{-1}) + 0.7927
Correlation coefficient (r)	0.9991
LOD (ng/ml)	6.29
LOQ (ng/ml)	20.99
RSD[a] (%)	0.35–0.93
Recovery (%)	98.0–101.4

[a] RSD = relative standard deviation.

Table 5
Recovery data obtained by standard addition method for (INH) in drug formulation.

Formulation	[Tablet] taken (ng/mL)	[Standard] added (ng/mL)	Found (mol L−1) (ng/mL)	Recovery (%)	RSD (%)
Isocid	6.8	4.08	10.74	99.4	1.02
	41.1	4.08	45.08	100.1	0.82
	82.2	4.08	86.20	100.2	0.24
	120.0	4.08	123.89	99.8	0.28

4. Conclusion

A carbon paste electrode in situ modified with surfactants was used for the improvement of the sensitivity towards the electrochemical measurement of an antituberculous drug (isoniazid). The effect of changing the pH of the solution, scan rate, stirring, the nature of surfactant (namely size, charge, and its concentration) on the electrochemical response are found to be a function of the improving process.

Spectrophotometric measurements showed that solution aggregates formation affect the surface interaction of the adsorbed species at the electrode surface and consequently the rate of charge transfer. NMR data gives a good expectation for the location and orientation of INH in different micelles and that the predominant interactions are columbic in nature and the secondary forces (hydrophobic) are less predominant on the electrochemical behavior. Also, the use of surfactants can be applied for the analysis of INH with a direct analytical procedure in aqueous media and in commercial tablets.

This study indicates that aromaticity, charge, and the chain length of surfactants are all complementary factors that depend on each other and cannot be neglected when we talk about surfactants.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.electacta.2010.11.034.

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