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ORIGINAL PAPER

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Voltammetric behavior of ethopropazine and the influence of sodium dodecylsulfate on its accumulation on gold electrodes

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Abstract Surfactants are sometimes used to improve the accumulation of some electroactive organic compounds, but anionic surfactants have seldom been utilized for such a purpose yet. In this paper, the influence of the anionic surfactant sodium dodecylsulfate (SDS) on the accumulation of ethopropazine (EPZ) at a polycrystalline gold electrode has been studied. EPZ exhibits an anodic peak at about 0.67 V (vs. SCE) and a shoulder in pH 3.5 citric acid–biphthalate buffer solution. In the absence of SDS, the peak is small and ill defined, but it becomes high and well shaped when SDS is added. This results from the adsorption of EPZ in the SDS membrane, which forms spontaneously on the gold electrode surface. For both cases EPZ shows the same electrode reaction mechanism, which is similar to that of promethazine (PMZ). The influence of other factors, such as pH value, variety and concentration of buffers, other surfactants, accumulation potential and time etc has been discussed. It was found that only the anionic surfactants had an enhancement effect on the EPZ accumulation. Also, the solution should be acidic or neutral so as to maintain the interaction due to its electrostatic nature. The optimum SDS concentration for EPZ accumulation is about 0.1 mM regardless of whether or not an accumulation potential is adopted. When all the experiment conditions are optimized, the peak current of the anodic peak changes linearly with the concentration of EPZ over the range 0.4–4 μM, and is thus of analytical significance.

Keywords Sodium dodecylsulfate · Ethopropazine · Gold electrode · Accumulation behavior

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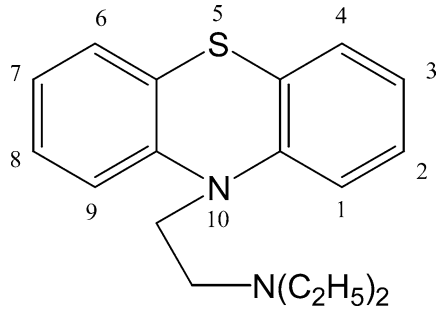
Introduction

Surfactants are often utilized in electroanalytical chemistry. In dc polarography, they are used to suppress the maxima; in ac polarography, they act as electrochemical masking agents [1, 2, 3, 4, 5]; in oscillopolarography [6] and others [7], they are introduced to enhance redox current. However, few anionic surfactants have been reported to improve directly the current response of electroactive organics. In this work, the anionic surfactant sodium dodecylsulfate (SDS) is investigated as an enhancing reagent for the anodic current response of ethopropazine (EPZ).

EPZ is a phenothiazine (PTZ) derivative substituted at the 10 position. Its molecular structure is shown in Scheme 1. PTZ derivatives, especially those substituted at the 10 or the 2 and 10 positions, are commonly known as antipsychotropic, anticholinergic and antihistaminic drugs. In addition, EPZ is mainly used to treat shaking palsy (i.e. Parkinson's disease). To study their action mechanism in the human body, electrochemical methods have some advantages, because they can supply information on electron transfer as well as concentration. The former is associated with the biological activity of PTZ derivatives. PTZ derivatives have been electrochemically studied using many kinds of electrodes such as Pt and Au electrodes [8, 9]. In some methods, hydrophobic electrodes such as the carbon paste electrode, and negatively charged membrane electrodes such as the Nafion modified glassy carbon electrode has been developed to accumulate and detect them [10, 11, 12, 13]. However, as is known, the Nafion film modified electrode cannot regenerate easily in detecting organic compounds, and the carbon paste electrode used is not a real solid electrode. Noble metal electrodes are easily treated solid electrodes, but they are usually ineffective for adsorbing organics so their detection sensitivities are generally not high. Obviously, the sensitivity is related to the accumulation to some extent. In this work the anionic surfactant SDS was investigated to improve the accumulation of EPZ.



Scheme 1 Molecular structure of ethopropazine

Experimental

Apparatus

Voltammetric studies were performed with a CHI 830 electrochemical analyzer (CH Instrumental Co., Shanghai, China) controlled by a personal computer. A three-electrode system was used, which included a gold working electrode, a platinum wire auxiliary electrode and a saturated calomel electrode (SCE) as reference electrode. The pH values were measured with a Mettler Toledo 320-S pH meter (Shanghai, China).

Reagents

EPZ was purchased from Sigma and chlorpropazine (CPZ) was obtained from Wujin Pharmaceutical Factory (China). The stock solutions (0.010 M) of them were prepared with *N*, *N*′-dimethylformamide (DMF) and absolute ethanol respectively. Both DMF and ethanol were proved to be of no obvious interference at a volume ratio lower than 10%. SDS, sodium dedecylbenzene sulfonate (SDBS), sodium dodecylsulfonate (SLS), dodecyltrimethylammonium bromide (DTAB), cetyltrimethylammonium bromide (CTAB) and cetylpyridinium bromide (CPB) stock solutions were prepared with a mixture of water and ethanol. Liquid surfactants including dodecyldimethylbetaine (BS-12), Triton X-100, Tween-80, Brij-35 etc. were all diluted with 99 volumes of water to make stock solutions. Other reagents used were of analytical or chemical purity. Double-distilled water was used in the preparation of all solutions unless indicated otherwise. The supporting electrolyte solution was a 0.050-M potassium biphthalate buffer solution adapted with citric acid to pH 3.5. The pH was adjusted using citric acid solution.

Electrode treatment

In order to get a clean and smooth electrode surface, the gold electrode (purity 99.99%, 2.0 mm in diameter, sealed in a Teflon tube) was polished with 0.3-μm Al_2O_3 slurry on a polishing pad, rinsed with distilled water, and washed ultrasonically in water and ethanol respectively for 1 min. Then the process was repeated, but this time 0.1-μm slurry was used. The resulting electrode was put in the cell for the experiment without further cleaning.

Procedure

10 ml of citric acid–biphthalate buffer (0.05 M, pH 3.5) together with an appropriate amount of EPZ and SDS stock solution was transferred to an electrochemical cell. Then the electrode system was put in the cell and the stirrer was turned on. After an accumulation of several minutes, the voltammograms were recorded from 0 to 0.9 V (vs. SCE) at a scan rate of 0.1 V/s. All measurements were performed at room temperature.

Results and discussion

Cyclic voltammograms of EPZ

The voltammograms of many PTZ derivatives have been studied [8]. Among them promethazine (PMZ) and CPZ are the most popular objects. As expected, the voltammetric behavior of EPZ is almost the same as that of PMZ as their molecular structures are very similar. But it is different from that of CPZ, which can be ascribed to different chain lengths between the two nitrogen atoms that are situated in the mother substance (phenothiazine) and in the side chain [14]. At pH 3.5, the voltammograms of EPZ are shown in Fig. 1, which is very

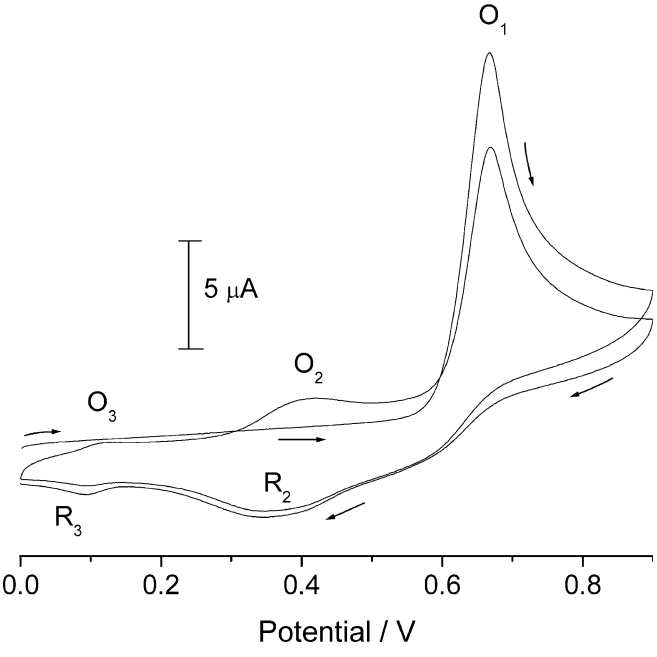


Fig. 1 Voltammograms of 0.5-mM EPZ on an Au electrode in 0.05-M potassium biphthalate buffer solution (pH = 3.5). Scan rate = 0.1 V/s, $t_a = 0$

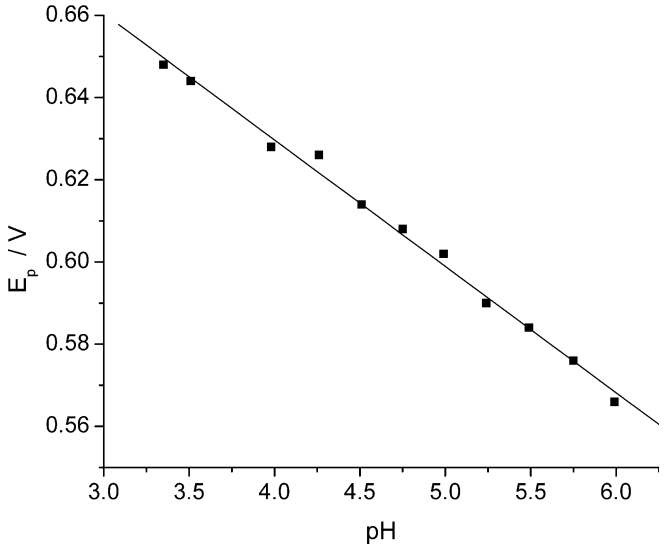


Fig. 2 Variation of peak potential with solution pH. Solution conditions: 0.1-mM EPZ + 0.05-M potassium biphthalate solution, $t_a = 0$

similar to that of PMZ [14]. An oxidation wave (O_1) can be observed on the initial scan. Following this two pairs of peaks corresponding to two couples (O_2/R_2 and O_3/R_3) appeared. Unlike CPZ, the peak potential of peak O_1 is pH dependent. As shown in Fig. 2, the peak potental shifts in a negative direction with increase in pH. The slope is 30.8 mV/pH, closing to that of PMZ reported [10, 14] and the theoretical value for a two-electron and one-proton transfer reaction. Thus it can be concluded that the electrode reaction mechanisms of EPZ and PMZ are identical at least over the pH range of 3–6. The electrochemical reactions are summarized in Scheme 2.

Most of EPZ molecules are protonated at pH 3.5, so they are expressed as $EPZH^+$. $EPZH^+$ is electrochemically oxidized to a cation radical $EPZ^{+\bullet}$ (1). The $EPZ^{+\bullet}$ can turn directly into many products including 2,3-dioxoethopropazine (A) and 4-oxoethopropazine (B) etc (2) according to the literature [14]. However, most $EPZ^{+\bullet}$ radicals are oxidized further to the dication EPZ^{2+} (3), which immediately transforms into A and B as well as sulfoxide (S) (4). The peak potential corresponding to (3), however, is lower than that of (1), so most protonated EPZ ions ($EPZH^+$) are oxidized to EPZ^{2+} in one step (5) [10, 14]. That is why only one peak is observed on the initial scan. In addition, some author have argued that $EPZ^{+\bullet}$ can disproportionate to 50% EPZ and 50% EPZ^{2+} (6) [9, 14], but the probability is small in the limited time span of the scan process.

$$EPZH^+ \rightarrow EPZ^{+\bullet} + H^+ + e^- \quad (1)$$

$$EPZ^{+\bullet} \rightarrow A + B + \ldots \quad (2)$$

$$EPZ^{+\bullet} \leftrightarrow EPZ^{2+} + e^- \quad (3)$$

$$EPZ^{2+} \rightarrow S + A + B + \ldots \quad (4)$$

$$EPZH^+ \rightarrow EPZ^{2+} + H^+ + 2e^- \quad (5)$$

$$2EPZ^{+\bullet} \leftrightarrow EPZ^{2+} + EPZ \quad (6)$$

Scheme 2 Electrochemical reactions of EPZ and PMZ

The shoulder, as we can see in Fig. 3b, is rather bewildering because it does not rise with the concentration of EPZ. That is to say, it is visible only when EPZ is at a low concentration (i.e. < 5 μM). At a high concentration (i.e. > 10 μM), the shoulder is covered by the peak of (5) as shown in Fig. 1. So it remains undetermined. More important, the ill-defined voltammogram of EPZ is not suitable for its determination at low concentrations. So to enhance the accumulation of EPZ at the electrode is the problem we should solve. In this work, we add the anionic surfactant SDS for this purpose. As we can see in Fig. 3c, when SDS is added to the solution, the peak of EPZ becomes well shaped and suitable for detection. As it is difficult for SDS to react with EPZ or its products, we cannot attribute the effect to a catalytic cycle. So the more effective accumulation of EPZ in the SDS membrane rather than the facilitation [15] of the membrane for the electrochemical reactions should account for this phenomenon.

Influence of solution pH and buffer solutions

Solution pH is one of the variables that strongly influences the shape of voltammograms and hence was investigated. Acidity is helpful for the protonation and stabilization of EPZ, but DS^- (dedecylsufate ion) also protonates to form dodecyl sulfuric acid in a strongly acidic medium. It was observed that the anodic peak of

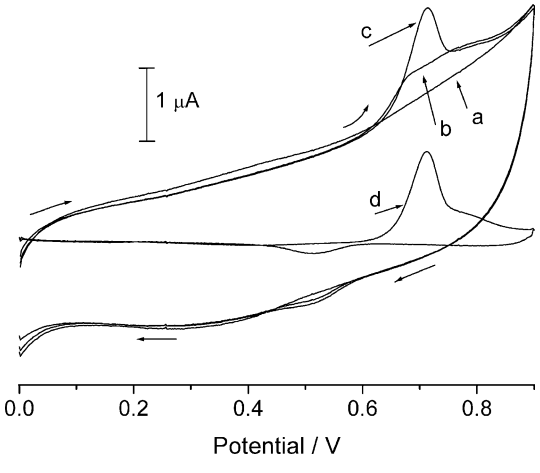


Fig. 3 Voltammograms of EPZ on the Au electrode. **a** 0.05-M potassium biphthalate buffer solution (pH = 3.5); **b**, **a** + 1 μM EPZ; **c**, **b** + 0.1 mM SDS; **d** the subtractive response **c**−**a**. Accumulation at open circuit, $\mathbf{t}_a = 2$ min, other conditions are as for Fig. 1

1-μM EPZ achieved the maximum current and best shape at pH 3.5 in the presence of 0.1-mM SDS, and 0.05-M citric acid–biphthalate buffer solution was the most suitable base solution. Other kinds of buffer solutions of the same concentration were also tested, such as phosphate buffer solution, HAc–NaAc, chloroactic acid–NaOH, citric acid–NaOH, sulfosalicylic acid–NaOH etc., but none of them was better than citric acid–biphthalate buffer solution. Nevertheless, these solutions showed little difference in this case, indicating that the interaction between EPZ and SDS and not the electrolyte caused the enhancement of accumulation of EPZ.

Influence of the concentration of base solution and other electrolytes

The dependence of peak current upon the concentration of biphthalate buffer solution and some ordinary salts was examined. It was observed that the current rose slightly with the reduction of buffer concentration. Taking into account the buffer capacity, a 0.05-M buffer was selected. The ordinary salts used, such as $CaCl_2$, NaCl, LiCl, KCl, K_2SO_4, Na_2SO_4, $KClO_4$, KBr, $NaNO_3$, and KNO_3, exhibited similar behavior. That is, the more they were added, the smaller the peak current was. Their influence is mainly due to the competitive adsorption of the cations with EPZ, since bivalent metal ions (e.g. Ca^{2+}) have a greater effect than monovalent ones (e.g. Li^+, Na^+, K^+). However, salts with the same cation showed no distinct difference. Halide ions, however, severely interfered with the measurement of peak current when their concentrations were higher. For example, when the concentration of Cl^- is above 0.5 mM, it will cause an anodic peak in almost the same potential region as EPZ after 2 min of accumulation. That is to say halide ions of higher concentration will interfere with the study of EPZ.

Variation of peak current with accumulation potential

Figure 4 shows the variation of peak current with accumulation potential from −0.6 to 0.2 V. Obviously, a negative potential is favorable for accumulation due to the electrostatic attraction force between the negatively charged electrode surface and the positively charged $EPZH^+$. Nevertheless, the peak current decreases when the accumulation potential is lower than −0.4 V, which can be partly attributed to the reorientation of the SDS membrane on the electrode surface [16]. A potential of −0.4 or −0.3 V, according to Fig. 4, is the best potential for accumulation. To our disappointment, detection limits for both accumulations at certain potential (e.g. −0.4 V) and at open circuit show little difference (80 nM for −0.4 V and 70 nM for open circuit). In view of the interference caused by the oxidation of coexistents that were reduced during the accumulation, an open circuit was selected for accumulation.

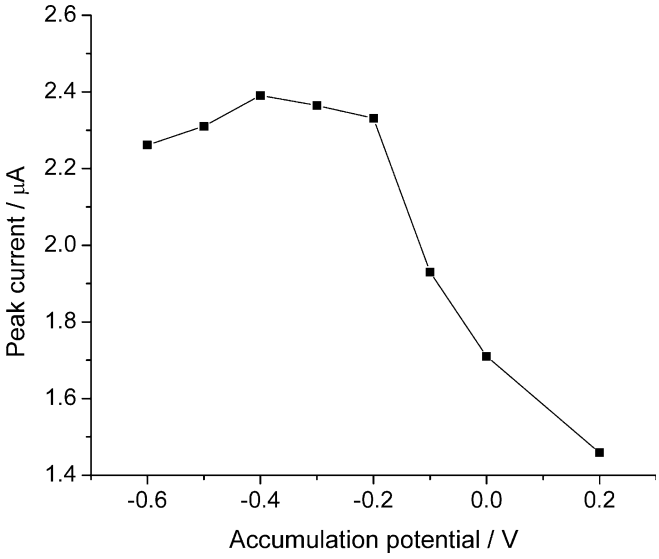


Fig. 4 Influence of accumulation potential on peak current of EPZ. Other conditions are as for Fig. 3c

Influence of surfactants upon accumulation

Many kinds of surfactants have been studied including the anionic surfactants SDS, SDBS, SLS, the cationic surfactants DTAB, CTAB, CPB and the nonionic surfactants Triton X-100, Tween-80, Brij-35 together with the ampholytical surfactant BS-12. Only anionic surfactants are favorable for accumulation in this case, and there is no obvious distinction between them. In contrast to anionic surfactants, other surfactants hinder the accumulation of EPZ to some extent. In addition, the enhancement action of SDS disappeared when the pH value increased to above 9.5 due to the deprotonation of $EPZH^+$. In accordance with these observations, we can conclude that the electrostatic action between DS^- and $EPZH^+$ is the prerequisite for the enhancement of accumulation. To our knowledge, surfactants used to improve the current of electroactive compounds are generally cationic, and the corresponding solutions are usually basic. Under basic conditions, the compounds are electronegative due to the dissociation of their carboxyl groups [17, 18] or the phenylhydroxyl groups [19] and can associate with cationic surfactants. It should be pointed out that the organic compounds we referred to do not include the metal complexes. Coordinating with metal ions will change the charge sign of the organic compounds, making it possible for them to associate with the anionic surfactants [6, 20].

Influence of SDS concentration upon accumulation

As shown in Fig. 5, the peak current of 1-μM EPZ reaches the maximum when the SDS concentration is in the range of 75–100 μM no matter what the accumulation potential is. If the concentration of SDS is too low, the membrane cannot form finely, and thus the current

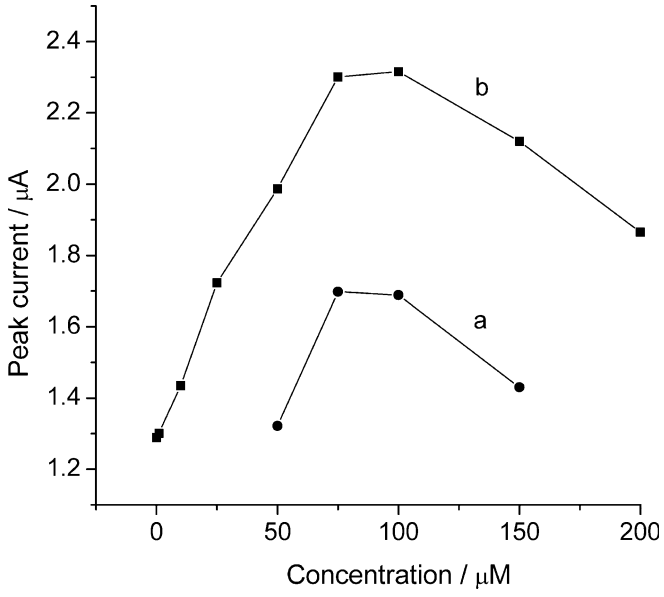


Fig. 5 Dependence of peak current of EPZ on concentration of SDS. Accumulation at **a** open circuit and **b** −0.3 V, other common conditions are as for Fig. 3c

of EPZ is smaller. On the other hand, the accumulation amount is also dependent on the concentration of $EPZH^+$. When SDS is added, the concentration of $EPZH^+$ will decrease due to its association with DS^- (to form $[EPZH(DS)_n]^{(n-1)-}$). So the greater the bulk concentration of SDS is, the smaller the $EPZH^+$ concentration will be. That is why the current reduces when the concentration of SDS is above 10 mM.

Interaction between electrode surface, SDS and EPZ

Surfactants can aggregate spontaneously on a gold surface mainly due to the hydrophobic interaction. Its aggregation morphology is related to the potential of gold and it transforms near the pzc (point of zero charge) of the gold surface [21, 22, 23] and at some negative potentials [16]. At a potential lower than the pzc but not too low, SDS aggregates on Au (111) as a hemi-cylindrical micellar monolayer. At a polycrystalline gold surface, the aggregation form of SDS may be different, and the pzc is not known either in the solution. However, it is certain that the sulfate head of SDS should be oriented towards the solution. It is unstable for the hydrocarbon tail groups to be exposed in solution because the surface energy cannot be greatly reduced when the sulfate head group adsorbs onto the surface, though gold have been proved to be hydrophilic in vacuum [24]. A gold electrode is electronegative and repels the sulfate group at open circuit. So does a gold electrode at about −0.3 V. This means that, if the potential is not too low, the aggregation morphology of SDS on the gold surface is similar no matter what the accumulation potential is. In other words, the adsorption morphology is not determined by the accumulation potential but by the SDS concentration.

The interaction between protonated organic compounds and surfactants with the opposite charge has been widely investigated before, and it has been utilized to improve the detection sensitivity of some drugs [25]. In solution, the concentration of dissociating $EPZH^+$ decreases in the presence of SDS. This accounts for the decrease in current for EPZ without accumulation when SDS is added, while the situation was reversed when an accumulation of more than 30 s was carried out, due to the adsorption of $EPZH^+$ on the electronegative SDS membrane, which forms spontaneously on the electrode surface when the solution is stirred. The interaction between $EPZH^+$ and DS^- on the electrode surface is the same as that in solution. The reason for EPZ adsorbing onto the electrode surface from solution is that the "concentration" of SDS in the membrane is higher than in the solution.

Hydrophobic interaction, being a basic intermolecular interaction, plays an important role in the association between surfactants and organic compounds in addition to the electrostatic force. It makes the association stronger. One fact is that we cannot find an obvious accumulation effect of SDS for epinephrine and dopamine. After all, the more kinds of forces there are, the stronger the interaction between SDS and EPZ, and the stronger the interaction between them, the more effective accumulation will be.

Effect of accumulation time on peak current

The effect of accumulation time has been investigated in the absence and presence of the SDS. The peak current of EPZ increased linearly with accumulation time over the range of 10–90 s (Fig. 6a) in the absence of SDS and 10–120 s in the presence of the SDS (Fig. 6b). When the

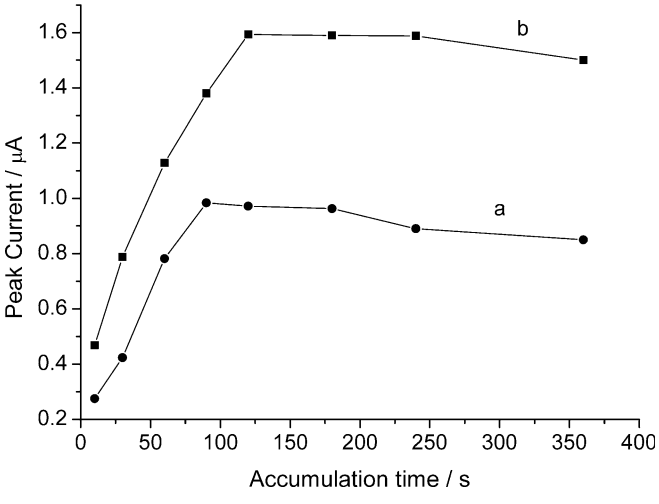


Fig. 6 Influence of accumulation time on peak current of EPZ in the absence (**a**) and presence (**b**) of 0.1-mM SDS, other common conditions are as for Fig. 3b

accumulation time exceeds these time spans, the current decreases slowly maybe due to slow chemical corruption of EPZ.

Dependence of anodic peak current on the concentration of EPZ

The dependence of peak current on the concentration of EPZ in the range of 0.1–800 μM has been studied and the plot has been made. It was observed that the current changed linearly with EPZ concentration over the range 0.4–4.0 μM with a correlation coefficient of 0.9992. At higher concentrations, the diffusion current of EPZ increased and became the main part of the current. As a result, the linearity occurred only in a low concentration range.

Conclusions

Surfactants had been proved to be useful in the accumulation of some organic compounds. In this study, the anionic surfactant SDS has been added to the solution to improve the accumulation of the drug EPZ at a polycrystalline gold electrode. The voltammetric behavior of EPZ has been investigated carefully and the oxidation mechanism has been summarized according to the literature and our investigation. EPZ shows a single well-shaped peak in a potassium biphthalate buffer solution of pH 3.5 at high concentration, but an ill-shaped one at low concentration. When 0.1-mM SDS is added to the solution, an SDS membrane forms spontaneously on the gold surface. Then the protonated EPZ ions are adsorbed in the membrane and the accumulation is enhanced, due to electrostatic and hydrophobic effects. As a result, the anodic peak of EPZ becomes well shaped, accompanied by an enhancement of current. It is of analytical value.

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