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Bismuth film electrode for stripping voltammetric measurement of sildenafil citrate

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ABSTRACT

A simple and fast procedure for measuring low concentration of sildenafil citrate (SC), also known as Viagra®, at the ex situ prepared bismuth film electrode (BiFE) is demonstrated. The BiFE was prepared ex situ on the surface of a glassy carbon substrate electrode and employed in adsorptive cathodic stripping voltammetric mode in 0.1 M acetate buffer solution (pH 4.5) in the presence of dissolved oxygen. Electroanalytical properties of the BiFE were studied and compared with the ex situ prepared mercury film electrode, lead film electrode and with bare glassy carbon electrode. The BiFE revealed a LoD (3σ) of 1.8×10^{-8} mol L^{-1} using 120 s accumulation time and good linear response in the examined concentration range of 1.0×10^{-7} to 1.0×10^{-6} mol L^{-1} SC with a correlation coefficient (R^2) of 0.995 using short accumulation time of 30 s. The obtained very good repeatability of 1.5% ($c = 1.0 \times 10^{-6}$ mol L^{-1}, $n = 15$) corroborated potential applicability of the BiFE for measuring SC, for example in pharmaceutical formulations. A successful preliminary study using constant current chronopotentiometric stripping mode has been also carried out.

1. Introduction

Recently, sildenafil citrate (SC, also Viagra®), a trivial name for 1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1-H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxy-phenyl]sulfonyl]-4-methyl-piperazine citrate (Fig. 1) has attracted considerable attention due to its application for oral therapy of erectile dysfunction. Initially it was investigated for its use in the case of hypertension and angina pectoris [1].

The measurements of SC are usually carried out by means of techniques such as liquid chromatography [2–8] or spectrophotometry [9,10] with appropriate sample preparation and time consuming SC pre-concentration. On the other hand, electrochemical techniques offer an attractive approach for direct, fast, simple and inexpensive measurements of electroactive organic and inorganic species, particularly in combination with stripping protocols which enable unique pre-concentration of the analyte in/on the surface of the selected working electrode. Hence, in the last few years, several attempts were taken to measure SC electrochemically using different types of electrodes and methods, e.g. SC was voltammetrically oxidized at boron-doped diamond electrode [11,12] and at glassy carbon electrode [13], reduced at hanging mercury drop electrode [14,15] and at the in situ prepared lead film electrode [16], and measured with electrochemical DNA biosensor [17]. Among these electrode materials, lead and mercury are well-known as toxic heavy metal pollutants being the latter associated also with significant difficulties in its handling, disposal, and subjected to very strict regulations.

Approximately one decade ago, bismuth film electrode was introduced as an alternative to its mercury counterpart and has been already widely accepted in numerous electroanalytical laboratories [18]. Namely, bismuth has been recognized as a “green” element exhibiting comparable electroanalytical performance to that of mercury. By now, bismuth electrodes have been used in different configurations, e.g. bismuth film electrode prepared on a glassy carbon [19], carbon paste [20], carbon fiber [21] or boron-doped diamond substrate electrode [22], bismuth oxide and bismuth powder bulk modified carbon paste electrodes [23,24], screen printed electrode [25], bismuth sputtered electrode [26] and bismuth bulk electrode [27], used for measuring inorganic [28–30] and organic analytes [31–34]. However, there is only a small number of works reporting on the application of the bismuth film electrode for measuring organic analytes in combination with the electrochemical stripping analysis, i.e. including the pre-concentration step [32].

In this work, we presented the successful application of the ex situ prepared bismuth film electrode (BiFE) for measuring low concentration levels of SC in combination with adsorptive cathodic stripping voltammetric mode in a non-deaerated 0.1 M acetate buffer solution.

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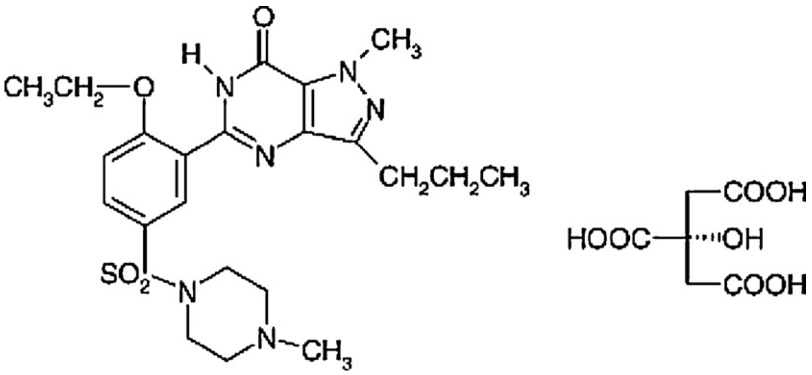

Fig. 1. Structural formula of sildenafil citrate.

2. Experimental

2.1. Apparatus

All measurements were performed using a modular electrochemical system AUTOLAB PGSTAT12 (Eco Chemie, Utrecht, Netherlands) in combination with GPES software (Eco Chemie). The usual three-electrode configuration was employed with the bismuth (BiFE), mercury (MFE) or lead film electrode (PbFE) all prepared ex situ on a glassy carbon (GCE) disk ($d = 2$ mm) as the working electrode, an Ag/AgCl/KCl (satd.) reference electrode and a platinum wire as the counter electrode. A computer controlled magnetic stirrer rotating at approximately 300 rpm was employed during the accumulation step. All experiments were carried out at room temperature of 23 ± 1 °C in a 20 ml voltammetric cell.

2.2. Reagents and solutions

All chemicals were of analytical grade purity. The standard solutions of bismuth(III), mercury(II) and lead(II) were provided by Merck and further diluted as required, whereas Sildenafil Citrate (SC) was obtained from LGC Standards (Germany). A stock standard solution of 1×10^{-3} M SC was prepared in water and stored at 4 °C. If not stated otherwise, a 0.1 M acetate buffer solution with pH 4.5 was used as a supporting electrolyte. Water used throughout the work was first deionized and then further purified using Elix 10/Milli-Q Gradient unit (Millipore, Bedford, USA).

2.3. Preparation of the BiFE, MFE and PbFE

The bismuth film electrode was prepared ex situ on the surface of a glassy carbon substrate electrode. Prior to plating, the glassy carbon electrode was polished with a 0.05 μm alumina slurry on a polishing pad. The electrode was then rinsed thoroughly with water and placed in a plating solution consisting of a 0.1 M acetate buffer (pH 4.5) and 5 mg L^{-1} Bi(III). A constant potential of −1.0 V was applied to the working electrode for 60 s while the solution was maintained under stirring conditions. After the modification step, the electrode was rinsed with purified water and ready to use. MFE and PbFE were prepared using a similar procedure, except that the plating solutions consisted of 10 mg L^{-1} Hg(II) in 0.01 M HCl for MFE and 20 mg L^{-1} Pb(II) in 0.1 M acetate buffer solution (pH 4.5) for PbFE. The potential of −0.6 V was applied for 300 s in the case of MFE and −1.2 V for 120 s in the case of PbFE.

2.4. Measurement procedures

If not stated otherwise, measurements were carried out using the cathodic stripping voltammetric mode. An accumulation potential of usually −0.6 V was applied to the working electrode for a definite period of time. After the equilibration period of 10 s, a stripping voltammogram was recorded using a square-wave potential scan with a frequency of 25 Hz, an amplitude of 50 mV, and a step potential of 4 mV.

3. Results and discussion

It has been proposed that the anodic voltammetric signals of SC at the bare GCE, recorded at ca 1.0 V and 1.2 V vs. Ag/AgCl in acetate buffer solution (pH 4.7) containing 30% of acetonitrile, are attributed to the oxidation of the piperazine ring of the SC molecule [13]. For the cathodic processes, observed at the mercury electrode at approximately −1.05 V and −1.15 vs. Ag/AgCl in 0.01 M $HClO_4$ (pH 2) [14], and also at the GCE at ca −1.4 V [13], the reduction of the sulfonyl group was suggested by Rodriguez et al. [14,15], but opposed by Zuman et al. [13], yet neither of these claims were supported by a clear experimental evidence. Our initial experiments were focused on the comparative examination of SC using cyclic voltammetry in combination with the bare glassy carbon electrode and the ex situ prepared bismuth film electrode with the potential scanning in the negative direction in the range of −0.3 V to −1.5 V. As can be seen in Fig. 2, two cathodic peaks were obtained at both electrodes at nearly identical peak potentials, i.e. at −1.26 V and −1.40 V at the bare GCE (dashed line), and at −1.25 V and −1.40 V at the BiFE (solid line) indicating the same totally irreversible reduction electrode processes. In this case, the BiFE exhibited a higher signal vs. GCE at −1.26 V, however, the smaller signals obtained at more negative potential of −1.40 V were associated with lower reproducibility. It is important to note, that when switched to cathodic stripping voltammetric mode, the GCE revealed also significantly lower reproducibility.

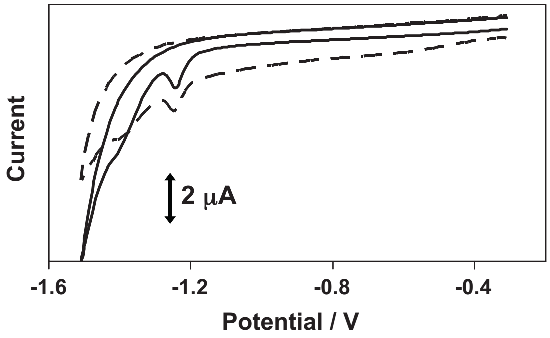

Fig. 2. Cyclic voltammograms of 5.0×10^{-6} mol L^{-1} SC at the ex situ prepared BiFE (solid line) and at bare GCE (dashed line) in 0.1 M acetate buffer solution (pH 4.5) purged with argon before measurement. Scan rate: 100 mV s^{-1}.