



Short communication

## Electrochemical determination of sildenafil citrate as standard, in tablets and spiked with human serum at gold and cystein modified gold electrode



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### ARTICLE INFO

#### Article history:

Received 15 July 2016

Received in revised form 20 September 2016

Accepted 11 October 2016

Available online 13 October 2016

#### Keywords:

Sildenafil citrate

Au/Cys electrode

Human serum analysis

Surface microscopic analysis

### ABSTRACT

Nonmedical use of sildenafil citrate (SC) requires new methods for drug determination in human serum and in tablets. SC as standard and in Sildenafil® tablets is determined by square wave voltammetry (SWV) in 0.1 M H<sub>2</sub>SO<sub>4</sub> (harmful for human serum) at gold electrode in a range: (1 × 10<sup>-3</sup>, 1 × 10<sup>-2</sup>, 0.1, 0.5, 1) μM and on cysteine (Cys) modified gold electrode (Au/Cys) in a range: (1 × 10<sup>-3</sup>, 1 × 10<sup>-2</sup>, 0.05, 0.1) μM. The presence of Cys causes two times larger peak currents and shifting of the incipient potential of the SC oxidation to 0.1 V in negative direction. A safe procedure for SC determination as standard and in Sildenafil® tablets spiked with human serum is developed by SWV at gold electrode in 0.05 M NaHCO<sub>3</sub> (suitable for human liquids) in a range: (1 × 10<sup>-3</sup>, 1 × 10<sup>-2</sup>, 0.1, 0.2, 0.3) μM. Microscopic characterization of the surfaces morphology was also performed. The SC concentrations were checked by high performance liquid chromatography-ultraviolet spectroscopy (HPLC-UV) showing that electrochemical method is more sensitive and can be used for the measurements of very low concentrations of the analyte.

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### 1. Introduction

In a treatment of erectile dysfunction (efficacy for antidepressant associated sexual dysfunction), pulmonary arterial hypertension and altitude sickness [1,2], oral phosphodiesterase (PDE) inhibitors are the first option. Three main PDE inhibitors are sildenafil, tadalafil, and vardenafil [3]. SC, which is chemically 1-[(3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl) sulfonyl]-methyl piperazine citrate (Fig. 1) attracts much attention.

Nonmedical use of SC has increased over the years [4,5]. SC treats and recovery of extreme tiredness after a long flight [6]. The most common adverse effects of sildenafil use included nasal congestion, impaired vision (blurriness, loss of peripheral vision, photophobia) and headache. Serious adverse effects include severe low blood pressure, heart attack, stroke, increased intraocular pressure, sudden hearing loss [7].

Protease inhibitors (treatment for HIV) inhibit metabolism of SC, effectively multiplying SC plasma levels, increasing the incidence of side effects [8]. For patients who are taking nitroglycerin or erythromycin,

who have decreased liver or/and renal function, low blood pressure, SC may be quantified in plasma, serum or whole blood to toxic level. That's why development of fast and safe methods for quantifying SC in plasma or serum is of great importance. Its determination in tablets requires also new procedures.

Analytical methods for the determination of SC concentration include spectrometric, chromatographic and electroanalytical methods [3]. Spectrometric methods include UV–VIS spectrophotometric [9] and spectrofluorimetric methods [10], NMR spectroscopy [11] and electrospray tandem mass spectrometry [12]. Examples of HPLC and gas chromatography comprise: liquid chromatography–electrospray–mass spectrometry (MS) [13], ultra-performance liquid chromatography with tandem MS [14–16], HPLC coupled with electrochemical detection [17], HPLC with UV detector [18], rapid resolution reversed-phase HPLC with diode array detector [19] and gas chromatography coupled with MS [20].

In electrochemical methods different electrodes and voltammetric techniques were used. The SC determination at pH 2.0 was performed by SWV and adsorptive stripping techniques at hanging mercury drop electrode [21]. At glassy carbon electrodes (GC), cyclic voltammetry and SWV were applied in determination of SC in the mixture with paracetamol and carvedilol [22] and in biological and pharmaceutical

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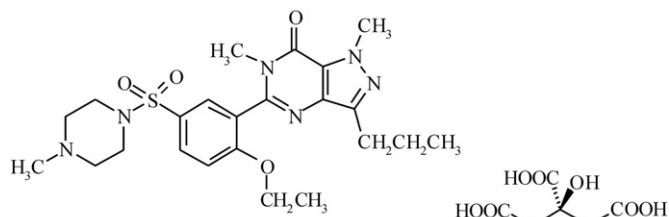


Fig. 1. Structural formula of sildenafil citrate.

formulations [23]. The cyclic and linear sweep voltammetric methods as well as differential pulse voltammetry (DPV) and SWV at GC were applied for oxidative determination of SC in solutions containing 30% (v/v) acetonitrile at different pH [24]. By SWV at Pb film modified GC a new method for determination of SC is developed [25].

Using DPV and SWV at boron-doped diamond and at diamond paste electrodes SC was determined [26,27]. GC was modified with a chitosan-supported ruthenium film in order to prepare sensor for SC [28].

The aim of this work is to develop a fast and safe SWV method for SC determination at gold electrode. Since acid electrolyte is harmful for human serum, SC was successfully determined as standard and as a content of Sildenafil® tablets at gold and at Au/Cys electrode in 0.1 M H<sub>2</sub>SO<sub>4</sub>. Additionally, SC was determined as standard and in Sildenafil® tablets spiked with human serum at gold electrode in 0.05 M NaHCO<sub>3</sub> respecting that the concentrations are in accordance with clinical serum level. Microscopic characterization of the surfaces morphology was performed using optical microscope. The SC concentrations in electrolytes were confirmed by HPLC-UV.

## 2. Experimental

### 2.1. Chemicals

Sildenafil citrate, provided by Hemofarm A.D. Stada, was used as SC standard and as content of Sildenafil® tablets (pharmaceutical formulation) with excipients: lactose monohydrate, cellulose, microcrystalline, hydroxypropylcellulose, croscarmellose sodium, sodium stearyl fumarate, silica colloidal anhydrous, Opadry II Blue, Opadry fx silver. L-cysteine, H<sub>2</sub>SO<sub>4</sub> and NaHCO<sub>3</sub> were purchased from Sigma Aldrich. De-ionized water was obtained from GenPure ultrapure water system (TKA, Niederelbert, Germany).

### 2.2. Electrochemical measurements

For SWV, PGZ 402 Volta Lab (Radiometer Analytical, Lyon, France) was used. The three electrode electrochemical cell and the preparation of polycrystalline gold electrode (surface area 0.5 cm<sup>2</sup>) were described in detail previously [29]. A gold wire was used as the counter electrode and a saturated calomel electrode (SCE) as the reference electrode. All potentials are given vs. SCE. The electrolytes were deoxygenated by purging with nitrogen.

### 2.3. Surface characterization

The surface characterization was performed using optical microscope (Olympus CX41) connected to the computer.

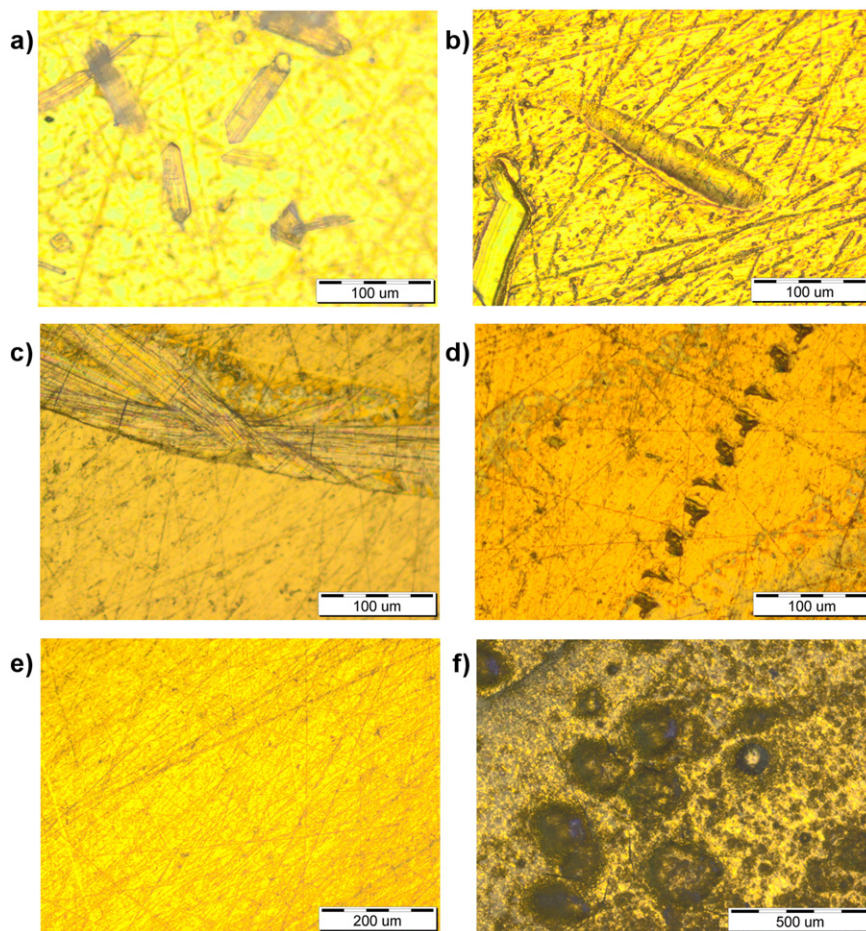


Fig. 2. Images obtained by optical microscope: a) SC standard on Au, b) Sildenafil® tablet on Au, c) SC standard on Au/Cys, d) Sildenafil® tablet on Au/Cys, e) serum on Au, f) Sildenafil® tablet spiked with serum.

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