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Fast analysis of terbutaline in pharmaceuticals using multi-walled nanotubes modified electrodes from recordable compact disc

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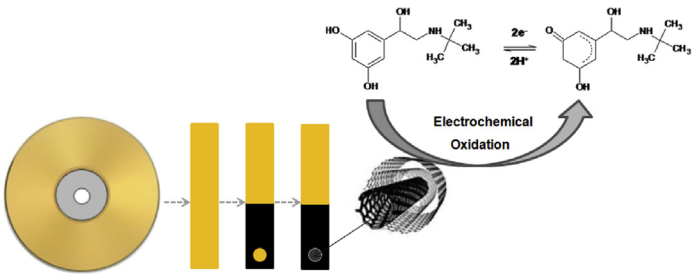
HIGHLIGHTS

- Gold CDs were modified for terbutaline determination in pharmaceutical samples.
- Functionalized carbon nanotubes were used to modify the surface of the gold electrodes.
- A flow electrochemical cell with impingent jet on the modified CD was used for amperometric detection of terbutaline.

GRAPHICAL ABSTRACT



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ABSTRACT

In this study, homemade disposable gold electrodes made from recordable compact disks were modified with carbon nanotubes for amperometric quantification of terbutaline sulfate in pharmaceutical products. A flow cell using an impingent jet of solution on the electrode surface was build and used for amperometric detection, and a series of experiments were carried out to find the best experimental conditions for the new electrode in a specially designed cell. A linear response for terbutaline was obtained in the range from 3.0×10^{-6} to 5.0×10^{-4} mol L^{-1} (at 0.63 V *vs.* Ag/AgCl). The limits of detection and quantification were calculated as 5.8×10^{-7} mol L^{-1} (S/N = 3) and 1.9×10^{-6} mol L^{-1} (S/N = 10), respectively. A frequency of 30 injections h^{-1} was attained. The proposed method was successfully applied to the analyses of commercial syrup samples, and all results were in good agreement with those obtained by using high performance liquid chromatography and capillary electrophoresis-tandem mass spectrometry.

1. Introduction

Terbutaline ((RS)-5[2-(tert-butylamino)-1-hydroxyethyl]benzene-1,3-diol) is a β_2 adrenergic receptor agonist used as a fast acting bronchodilator and anti-contraction agent during preterm birth [1]. The development of methods to quantify terbutaline is important for both the control of pharmaceuticals products such as inhalation aerosol, injectable solution, tablet, and liquid or syrup [2] and the clinical chemistry [3], for example, in cases of overdose. Even terbutaline being relatively stable, its degradation can generate different products, and this aspect is important in the case of pharmaceutical products. This process can be accelerated when exposed to solar irradiation, such as in natural water [4], or when

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used as feed additive to increase the production of lean meat in the livestock [5].

Different analytical methods for the determination of terbutaline sulfate are report in the literature. These methods include capillary electrophoresis (CE) coupled to mass spectrometry [6], high performance thin-layer chromatographic (HPTLC) [7], CE-electrochemiluminescence detection [8], radioimmunoassay [9], CE-UV detection [10], molecular phosphorescence spectroscopy [11], gas chromatography (GC) coupled to mass spectrometry [12], conductometry in batch and flow injection conditions [13], high performance liquid chromatography (HPLC) coupled to mass spectrometry [14] and UV spectrophotometry [15]. Many of the described methods require time-consuming sample preparation or expensive instrumentation.

Electroanalytical techniques possess many advantages over other techniques such as facility of use, simplicity, high sensitivity, and is low cost. Sensors based on carbon nanotubes (CNTs) have generated great interest since their discovery in 1991. CNTs (single-walled carbon nanotubes – SWCNTs and multi-walled carbon nanotubes – MWCNTs) sensors generally exhibit lower limits of detection, faster electron transfer kinetics, higher sensitivities, and larger surface area than conventional carbon electrodes [16]. Some electrode substrates have been modified with CNTs to obtain good electroanalytical results in different samples [16–18].

In this work, MWCNTs have been used to modify the surface of a gold electrode made from a recordable compact disk (CD-R) slice for terbutaline quantification in pharmaceutical products during amperometric analysis and under flowing regime. Modified gold electrodes were immersed in an electrochemical cell containing a lateral entrance. Amperometry associated with the wall jet process provide a simple way for the mechanization (or even automation) for routine analysis with elevated reproducibility and good sensitivity.

Gold working electrodes constructed from CD-Rs were first reported by our group [19] and have been used in different applications, such as determination of lead and copper in ethanol [20] and lubricating oil [21]; mercury in natural waters [22], fishes and shrimp [23] and urine [24] and in pharmaceutical products [25]. Strategies for the construction of disposable electrodes [26] and arrays of microelectrodes [27] were also developed. Some other applications include the use of gold CD-Rs to construct microchips for electrophoresis applications [28], electrodes for quantification of selenium [29], for the construction of electronic tongues [30], to build immunosensor for quantification of anti-*Trypanosoma cruzi* antibody [31], and to quantify mercury in fish samples, using chronopotentiometric stripping analysis [32].

2. Experimental

2.1. Reagents and solutions

MWCNTs (6–9 nm in diameter, 5 μm in length and 95% purity) was purchased from Sigma–Aldrich (Houston, USA). Acetic acid, boric acid, hydrochloric acid, dimethylformamide (DMF), sodium dihydrogen phosphate, and potassium mono-hydrogen phosphate were purchased from Merck (Darmstadt, Germany). The solutions were prepared with ultrapure water from a Millipore Milli-Q system with resistivity ≥18.2 MΩ cm (Barnstead, Dubuque, IA, USA). The stock solution of terbutaline sulfate (0.10 mol L^{-1}) was prepared by dissolving the solid salt in ultrapure water and stored in a dark flask under refrigeration. The standard solutions of the analyte were properly diluted with supporting electrolyte just before the measurements. The pharmaceutical formulations (*Bricanyl*® – syrup, fabricated by AstraZeneca do Brasil Ltda.) originated from different fabrication lots (32546-05/14 and 36311-04/15) were purchased in a local drugstore.

Two different supporting electrolytes were evaluated by cyclic voltammetry in experiments involving the oxidation of terbutaline sulfate: Britton–Robinson buffer (0.10 mol L^{-1}, pH 2.0–8.0) and K_2HPO_4/NaH_2PO_4 buffer solution (0.10 mol L^{-1}, pH 7.0–9.0). The phosphate buffer (pH 8.0) gave the best results and, then, it was adopted along for the next measurements. This buffer was prepared by mixing 0.086 mol L^{-1} K_2HPO_4 and 0.014 mol L^{-1} NaH_2PO_4.

2.2. Instrumentation

2.2.1. Cyclic voltammetry and amperometry

All measurements were performed using an EcoChemie PGSTAT-20 potentiostat (EcoChemie, The Netherlands). Cyclic voltammetric studies were performed using a conventional 5 mL electrochemical cell. In this study, the working electrode was always built with the same circular area with 4.0 mm diameter (area ~0.13 cm^2), delimited by a toner mask prepared by using the procedure described elsewhere [27]. The reference electrode was a miniaturized $Ag/AgCl_{(sat\ KCl)}$ built in our lab, and the auxiliary one was a platinum wire. The flow-amperometric experiments were performed using the flow cell depicted in Fig. 1. This 45 mL inner volume cell was constructed in Plexiglas. The three electrodes were placed in the electrochemical cell through holes in its cover. The surface of working electrode was positioned 3 mm far from of the outlet of the polyethylene tube. To assure a reproducible positioning, the sensor was firmly fixed in the cover of the cell. A peristaltic pump (Ismatec, Zurich, Switzerland) was employed for fluid propulsion. The manifold was built with polyethylene tubes. The standard solutions and terbutaline samples were introduced into the stream by a manually operated injection valve.

2.3. Nanotubes characterization

Transmission electron microscopy (TEM, JEOL JEM 2100, Peabody, MA, USA) was used to reveal the morphology of the modified MWCNT. TEM samples were prepared by depositing a drop of diluted suspension of functionalized MWCNT (1 mg/mL) in ultrapure water onto a holey film-coated copper grid. TG/DTA curves were performed in a TGA-50/DTA-50 Shimadzu (Kyoto, Japan) instrument under synthetic air (50 mL min^{-1}) at a heating rate of 5 °C min^{-1}. The sample mass of both purified and pristine MWCNTs were about 10 mg and were weighed to Pt crucibles.

2.4. Comparison techniques

Two methodologies (high-performance liquid chromatography (HPLC) and capillary electrophoresis-tandem mass spectrometry (CE-MS/MS) were used to compare the results obtained by the proposed method. The chromatograms were recorded on a LC-10 AS chromatograph (Shimadzu Co., Japan) equipped with UV–vis wavelength spectrophotometry detector (SPD-6AV) and a Phenomenex C18 chromatographic column (4.6 × 250 mm, 4 μm particle size).

The CE-MS/MS equipment was an Agilent 7100 coupled to a 6430 triple-quad mass spectrometer (Agilent Technologies, Santa Clara, CA, USA) equipped with an electrospray ionization (ESI)