Highly sensitive and selective polyaniline–zinc oxide nanocomposite sensor for betahistine hydrochloride in solubilized system

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A B S T R A C T

A sensitive electroanalytical method for the quantification of betahistine hydrochloride in pharmaceutical formulation has been developed on the basis of an enhanced electrochemical response at glassy carbon electrode modified with polyaniline–zinc oxide (PANI–ZnO). Results suggest that betahistine hydrochloride in sodium lauryl sulfate (SLS) exhibits an electrocatalytic effect resulting in a marked enhancement of the peak current. The electrochemical performance of the modified PANI–ZnO/GCE sensor was investigated by cyclic voltammetry and square wave voltammetry (SW). Calibration plot reveals linearity within the range 25–515 μg/mL with a correlation coefficient of 0.997. A lower limit of detection of 19.57 μg/mL proved the sensitivity of the proposed method.

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1. Introduction

Betahistine, N-methyl-2-(2-pyridyl)-ethanamine (A) is a medicine that closely resembles the natural substance histamine. It is an anti-vertigo drug first used for treating vertigo associated with Meniere's disease. It is also used for patients with balance disorders [1,2].

(A)
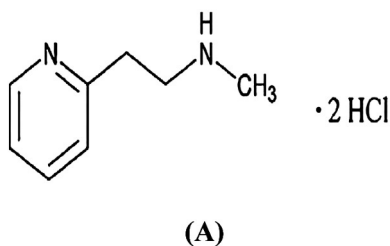
Electrochemical methods such as square-wave voltammetry (SWV), stripping voltammetry (SV), differential pulse voltammetry and cyclic voltammetry have been widely used for the determination of pharmaceuticals at the modified electrodes [3–8]. It has been observed that surfactants have great significance in electrode reactions and are widely used in electrochemical investigations. Surfactants heavily influence the redox process of electroactive species and improve the sensitivity

and selectivity [9,10]. Spectrophotometric methods and high performance liquid chromatographic (HPLC) procedures have been reported for the determination of betahistine hydrochloride [11]. Determination of betahistine hydrochloride in tablets and human urine has been performed by an amperometric detector in capillary electrophoresis [12], voltammetric assay method [13], potentiometric sensor method [14] and titration method [15]. However there is no report available regarding the electrochemical study of betahistine hydrochloride at PANI–ZnO/GCE electrode.

Electrochemical sensors and biosensors have attracted tremendous research interest, as they demonstrated its numerous applications in various fields, including pharmaceuticals, medical diagnosis, and environmental control [16–35]. Polyaniline (PANI) and its composites have a wide range of technological applications including storage batteries, electrochemical devices, light emitting diode, corrosion inhibitor and a variety of chemical and bio-sensors [36–39]. Nanosized ZnO, an important semiconductor, is used widely in preparing solar cells, gas sensors, catalysts, chemical sensors, electrical and optical devices, and electrostatic dissipative coatings [40,41].

Several studies have been conducted in recent years on the synthesis, characterization and application of PANI–ZnO nanocomposites. A dramatic improvement in the mechanical, thermal, electrical, optical, and redox properties of these nanocomposites is expected in comparison to components individually. However, to the best of our knowledge, the application of PANI–ZnO nanocomposite as a sensor for the determination of betahistine hydrochloride has not been reported yet. In the present study, PANI–ZnO/GCE nanocomposite synthesized by the interfacial method has been used to modify glassy carbon electrode.

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2. Experimental

2.1. Materials and methods

All chemicals used were of analytical reagent grade and employed without further purification. Aniline was used after distillation under vacuum. Aniline was obtained from RFCL Limited. Camphor sulfonic acid used as a doping agent was obtained from Ranbaxy, India. Zinc oxide nanopowder with 97% purity was obtained from Sigma Aldrich. Ultra pure water was obtained from Milli-Q purification system (Millipore Corp., Milford, MA, USA). Betahistine hydrochloride standard (98% purity) was obtained from RFCL Ltd., New Delhi, India. Tablets containing betahistine hydrochloride (Zevert) labeled 16 mg were obtained from commercial sources.

2.2. Pharmaceutical preparation

Betahistine hydrochloride (1.5 mg/mL) was dissolved in different solvents viz. acetonitrile (ACN), water, N,N-dimethylformamide (DMF), surfactants such as cetyltrimethylammonium bromide (0.1% CTAB), sodium lauryl sulfate (0.1% SLS) and 0.1% Tween-20. Solutions were sonicated for 15 min and centrifuged. Clear supernatant liquid was withdrawn. The solutions for recording voltammograms were prepared by mixing an appropriate volume of BR buffers, stock solution and KCl (1.0 M).

2.3. Instrumentation

Electrochemical measurements were performed using a μAutolab Type III (Eco-Chemie B.V., Utrecht, the Netherlands) potentiostat–galvanostat with a 757 VA Computrace software. The utilized electrodes were, PANI–ZnO material modified glassy carbon electrode as working electrode, Ag/AgCl (3 M KCl) as reference electrode and graphite rod as auxiliary electrode. All solutions examined by electrochemical techniques were purged for 10 min with purified nitrogen gas. All pH measurements were made on a Systronics digital pH model-361 meter fitted with a glass electrode and a saturated calomel electrode as reference, which was previously standardized with buffer solutions of known pH. SEM spectra of the nanocomposite films were recorded using a Zeiss EV0 50 SEM. Fourier transform infra-red (FTIR) spectroscopy (Shimadzu) of PANI–ZnO nanocomposite sensor was studied in the frequency range 400–4000 cm^{-1}. TGA of the nanocomposite films was performed using a TGA Q50 v6.7 Build 203 at a heating rate of 10 °C min^{-1} under nitrogen flow from 50 to 700 °C.

2.4. Preparation of PANI–ZnO nanocomposite sensor

The PANI–ZnO nanocomposite was fabricated by an interfacial polymerization method using ammonium persulfate as an oxidizing agent. Typical synthesis consists of the following steps, (i) 0.36 mL predistilled aniline was dissolved in 40 mL carbon tetrachloride (solution A), (ii) 0.456 g ammonium persulfate was dissolved in 0.1 M camphor sulfonic acid and stirred until a homogenous solution is obtained (solution B), (iii) 15% ZnO was added to solution B, and then solution A was added into mixture B with vigorous stirring for 10 min, (iv) solution obtained was kept at 4 °C overnight, polymerization reaction occurred at the interface of two immiscible solvents, and thus the (v) obtained PANI–ZnO precipitate was centrifuged for 5 min, washed with deionizer water and ethyl alcohol for several times and left at room temperature overnight for drying.

2.5. Fabrication of PANI–ZnO modified glassy carbon electrode

Prior to modification, the bare glassy carbon electrode (GCE) was polished with alumina powder of different particle sizes (0.05–0.3 μm), suspended in deionized water on a polishing cloth and thoroughly rinsed with double distilled water and ethanol, followed by sonication in an ultrasonic bath for 10 min. PANI–ZnO nanocomposite was dispersed in N,N-dimethylformamide (DMF), and ultrasonicated for 2 h to get a homogenous suspension [42]. 6 μL of the suspension was casted on the surface of freshly polished GCE (Scheme 1).

3. Results and discussion

### 3.1. Scanning electron microscopy (SEM)

PANI–ZnO composite was characterized by SEM images of polyaniline, ZnO and PANI–ZnO composite (Fig. 1). Fig. 1A shows that PANI has a rod like shape with some of these rods less than 100 nm in size, where nearly hexagonal particles of ZnO (Fig. 1B) in addition to polyaniline (Fig. 1A) resulted in PANI–ZnO composite (Fig. 1C) having nanoparticles of ZnO attached with polyaniline. It is observed that the composite is composed of different sized fibrillar structures. The fibrous structure of PANI and ZnO nanoparticles glued to PANI is clearly seen [43].

3.2. Fourier transform infrared spectroscopy studies (FTIR)

The incorporation of CSA and ZnO into the polymer chain was confirmed from the FTIR studies. The characteristic peaks at 1565, 1486, and 1244 cm^{-1} appear in the FTIR spectrum of the PANI–ZnO composites, shifting to higher frequency in comparison to the corresponding peaks of pure PANI at 1562, 1479, and 1243 cm^{-1} respectively [44–46].

3.3. Thermo gravimetric analysis (TGA)

From the TGA curve of polyaniline and PANI–ZnO composite, it can be seen that the thermal degradation of PANI occurs at 275 °C and the initial mass loss at lower temperature is mainly due to the
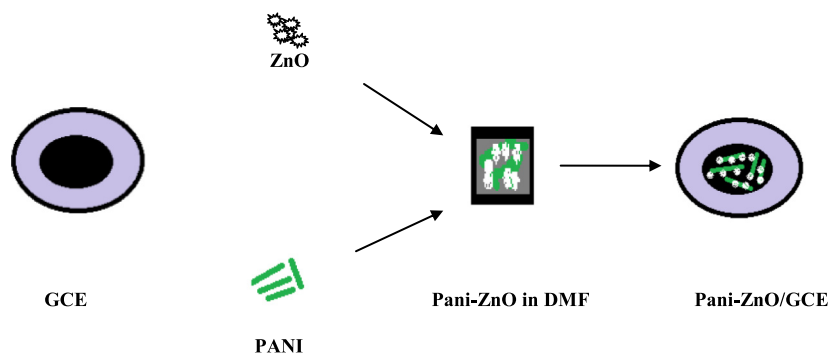
Scheme 1. Fabrication of the sensor.