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Gold nanoparticles decorated poly-melamine modified glassy carbon sensor for the voltammetric estimation of domperidone in pharmaceuticals and biological fluids

Rosy, Rajendra N. Goyal *

Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247667, India

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ABSTRACT

The electrochemical response of an unmodified glassy carbon (GCE), poly-melamine/GCE and gold nanoparticle (AuNP)/poly-melamine/GCE is compared in the present protocol for the sensitive and selective determination of domperidone (DOM). The AuNPs were synthesized in the laboratory and characterized using UV–visible spectroscopy and Transmission Electron Microscopy (TEM). Melamine was electropolymerized onto the glassy carbon surface using cyclic voltammetry and was investigated using Field Emission Scanning Electron Microscopy (FE-SEM) and Electrochemical Impedance Spectroscopy (EIS). The AuNP/poly-melamine/GCE exhibited the best electrochemical response among the three electrodes for the electro-oxidation of DOM, that was inferred from the EIS, cyclic and square wave voltammetry. The modified sensor showed a sensitive, stable and linear response in the concentration range of 0.05–100 μM with a detection limit of 6 nM. The selectivity of the proposed sensor was assessed in the presence of high concentration of major interfering molecules as xanthine, hypoxanthine, and uric acid. The analytical application of the sensor for the quantification of DOM in pharmaceutical formulations and biological fluids as urine and serum was also investigated and the results demonstrated a recovery of $>95\%$ with R.S.D of $<5\%$.

1. Introduction

Domperidone (DOM), or 5-chloro-1-[1-[3-(2,3-dihydro-2-oxo-1H-benzimidazol-1-yl) propyl]-4-piperidinyl]-1,3-dihydro-2H-benzimidazol-2-one (Fig. 1) is usually administered in the treatment of gastro esophageal reflux disease (GERD) and gastrointestinal motility disorders as DOM lowers esophageal sphincter pressure, stimulates antroduodenal motility and accelerates gastric emptying [1]. Antiemetic effect of DOM may be attributed to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, but unlike other dopamine antagonists DOM does not penetrate the blood brain barrier because of its high molecular mass, low lipid solubility and high protein binding [2–4]. Thus, DOM may be employed in the safe and selective way of assessing the role of peripheral dopaminergic activity for the treatment of nausea and orthostatic hypotension in Parkinson's disease, and patients undergoing cancer therapy without affecting the extrapyramidal symptoms [1,5,6]. By altering the dopamine concentration DOM indirectly affects the prolactin secretion and increases the lactation in females [4]. DOM has been approved by the American Academy of Pediatrics for inducing and increasing lactation and use in breastfeeding as a handful of studies have shown that DOM does not readily cross the placental barrier and very small amount of medication reaches to breast milk [4,7–9]. But now a days, the use of DOM for treating gastric problems is diminished as cases of severe ventricular arrhythmia and cardiac side effects have been reported along with studies showing that prolonged use of DOM results in sexual dysfunctions [10–12]. Thus, the detection of DOM in body fluids is of prime importance as its presence signifies the threat to cardiac arrest, increased lactation, sexual dysfunction and other dopamine imbalance related problems.

Conducting polymers have attracted much attention from the scientific community in this decade because of their unique electrical conductivity [13]. Melamine, a conducting polymer with amino groups is believed to adhere to the carbon surface, exploiting the oxygen functionalities and the defects of the electrode surface [14]. The nitrogen rich matrix of poly-melamine with plenty of π-electrons is supposed to interact with the pair of π-electrons residing on the tertiary nitrogen atom of the pyridine present in DOM [15]. Moreover, the amino groups of poly-melamine also served as the glue for the nanoparticles as it is well known that the interaction of gold nanoparticles (AuNPs) with the

* Corresponding author. Tel.: +91 1332 285794 (office).
E-mail address: rngcyfcy@iitr.ac.in (R.N. Goyal).

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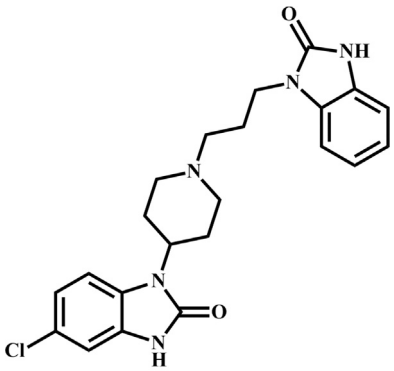

Domperidone

Fig. 1. Structure of domperidone.

basic nitrogen centers of the polymer backbone provides extra stability and results in increased deposition of nanoparticles [16,17]. Thus, the approach of using amino functionalized polymer film decorated with AuNP to provide electrocatalytic effect toward the electrochemical sensing has been investigated in the present study and is employed for quantification of DOM in biological fluids and commercially available pharmaceutical samples.

Enormous techniques like liquid chromatography–mass spectrometry (LC–MS) [18,19], high performance liquid chromatography (HPLC) [20,21], spectrophotometric methods [22,23], reverse phase HPLC [24,25] have been employed previously for the detection of DOM. Very few potentiometric [26] and electrochemical sensors [27,28] have also been reported in the last decade, but those involve a very superficial study of DOM. Recently we tried to develop a sensor for DOM determination using poly(4-amino-3-hydroxynaphthalene sulfonic acid) p(AHNSA) [29]. However, the electrocatalytic activity was assigned to increased surface area and electrostatic attraction of carbonyl group and NH_2 of DOM and amino and OH groups of p-AHNSA. To establish that sulfonic acid moiety of p-AHNSA does not participate in the electrocatalytic activity of DOM, in the present study electropolymerization of melamine which only amino groups has been carried out on a glassy carbon electrode (GCE). To further decrease the detection limit of DOM, AuNPs were also used. The electrochemical response of the modified sensor towards the DOM oxidation process was analyzed and compared with the response obtained using unmodified GCE.

2. Experimental

2.1. Reagents

Domperidone, $HAuCl_4 \cdot 3H_2O$, melamine, uric acid (UA), xanthine (X), hypoxanthine (HX), sodium citrate and $NaBH_4$ were purchased from Sigma-Aldrich (USA) and used as received. Phosphate buffers of ionic strength ($\mu = 1.0$ M) in the pH range 2.4–10.0 were prepared according to the method of Christian and Purdy [30]. All other chemicals and solvents used in the experiment were of analytical grade and double distilled water was used throughout the experiments. Human samples of serum and urine were collected from the hospital of I.I.T.Roorkee after taking the permission of the ethical clearance committee. Two commercially available pharmaceutical preparations named Domstal (Torrent Pharmaceuticals Ltd., Ahmedabad, Gujarat) and Domdis (Zorex Pharma Pvt. Ltd., Santej, Ahmedabad, Gujarat) were obtained from the local market of Roorkee.

2.2. Instrumentation

Bio-analytical system (BAS, West Lafayette, USA) CV-50W voltammetric analyzer was employed in all the voltammetric experiments. A conventional three electrode system was used, incorporating unmodified glassy carbon electrode (GCE, diameter = 3 mm) or AuNP/melamine/GCE as a working electrode, a 3 M NaCl, Ag/AgCl (BAS Model MF-2052 RB-5B) as a reference and Pt wire as an auxiliary electrode. The pH measurement of buffer solutions was performed using a digital pH meter (Eutech Instruments, model pH 700). UV–visible spectroscopy and Transmission Electron Microscopic measurements (TEM) were carried out using Perkin Elmer Lambda 35 UV–vis spectrometer and TEM model; Technai G2 20S-TWIN respectively. The topographical characterization of modified and unmodified sensors was carried out using Field Emission Scanning Electron Microscopy (FE-SEM, model; Zeiss Ultra plus 55). Electrochemical impedance spectroscopy (EIS) was done using a galvanostat (model; Versastat 3, PAR).

2.3. Preparation of gold nano-particle solution

A colloidal nano-gold solution was prepared by adding 1 mL of $HAuCl_4 \cdot 3H_2O$ (1 wt%) solution to 90 mL double distilled water. After stirring the above solution for 1 min, 2 mL of 38.8 mM sodium citrate was added to it and the solution was again stirred for 1 min. To this solution, 1 mL of freshly prepared 0.0075 wt % $NaBH_4$ solution (prepared in 38.8 mM sodium citrate) was added very slowly accompanied with continuous stirring. The addition of $NaBH_4$ was performed very carefully [31]. The solution was then permitted to stand for 15 min and then characterized using UV–visible spectroscopy and TEM for further applications.

2.4. Fabrication of AuNP/melamine/GCE sensor

Prior to modification, the surface of glassy carbon was manually polished to a mirror like finish with a paste of alumina powder (grade I) and ZnO on a micro-cloth pad and was rinsed with double distilled water. The electropolymerization of melamine was carried out on the polished surface of GCE in a solution of 10 mM melamine (prepared in 0.1 M H_2SO_4). The cyclic voltammograms were recorded by scanning the potential between 0 V and +1.6 V at a scan rate of 100 mV s^{-1} for 20 scans [32]. The film obtained was rinsed with double distilled water and allowed to dry at room temperature. To optimize the volume of AuNP, 2–15 μL was casted on the modified GC surface and voltammograms were recorded in 10 μM of DOM. The maximum peak current was observed when 10 μL of AuNP solution was drop casted onto the poly-melamine modified GC surface; therefore, it was selected as the optimum volume and was used throughout the experiment as modification protocol. The final sensing surface was obtained just after rinsing with double distilled water, which was characterized with the help of FE-SEM and used for further electrochemical studies.

2.5. Voltammetric procedure and sample preparation

For carrying out voltammetric studies, a stock solution of DOM was prepared by dissolving the required amount of DOM in a minimum volume of methanol (~2 mL) and then distilled water was used to make 25 mL solution. Test solutions were prepared by taking the required volume of the DOM solution in an electrochemical cell already holding 2 mL of pH 7.2 ($\mu = 1$ M) phosphate buffer as supporting electrolyte, and the solution was finally made to 4 mL using double distilled water. Voltammograms were then recorded by applying the following optimized parameters: initial potential (E): 400 mV, final potential (E): 1200 mV, square wave frequency (f): 15 Hz, square wave amplitude (Esw): 25 mV and potential step (E): 4 mV.