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Staircase voltammetric determination of 2-thiouracil in pharmaceuticals and human biological fluids at polyaniline and polypyrrole film modified sensors

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ABSTRACT

The conducting polymers like polyaniline(PA) and polypyrrole (PP) films modified graphite pencil electrodes (GPE) were used to determine the trace amounts of 2-thiouracil (2TU) in biological samples using cyclic and stair case voltammetric techniques. 0.1 mM each of aniline and pyrrole were successfully electropolymerized separately on GPE using cyclic voltammetry. Morphology of electrodes was characterized by AFM. The negative shift of oxidation potential compared to bare GPE, shows that the PA and PP modified electrodes had catalytic activity for the 2TU oxidation. The results showed that the electrochemical oxidation of 2TU on the modified electrodes was diffusion-controlled. The effects of pH, scan rate, concentration of 2TU and modifiers were optimized. Under optimized conditions, the electrodes showed a linear response in the range of $1.0 \times 10^{-8} - 1.5 \times 10^{-7}$ M for PP/GPE with a detection limit of 1.6×10^{-9} M and $1.0 \times 10^{-8} - 1.3 \times 10^{-7}$ M for PA/GPE with a detection limit of 1.8×10^{-9} M. The sensors were successfully applied to determine the trace amounts of 2TU in human biological fluids and pharmaceutical samples.

1. Introduction

2-Thiouracil (2TU) was the first thionamide anti-thyroid drug [1]. It occurs in seeds of Brassica and Crucifera species. 2TU has been identified in t-RNA and it plays an important role in antiviral and anticancer activites [2]. Thiouracil belongs to a class of drugs used in the treatment of hyperthyroidism which acts by interfering with thyroid peroxidase functioning, thus decreasing the production of thyroid hormone and increasing proliferation by increasing the concentration of thyroid-stimulating hormone [3]. It has been used in coronary vasodilator and in congestive heart failure. It is highly selective inhibitor of nitric oxide synthase (NOS) and also covalently binds dopaquinone, produced by tyrosinase catalyzed oxidation of tyrosine, thereby selectively accumulating in de novo-synthesized melanin in overactive melanin-producing cells and provide a means to localize melanoma cells [4,5]. The synthesis, structural studies, and an anti-HIV activity of some new complexes of metal ions of 2TU were recently reported [6]. Because of the biological importance of 2TU, the determination of 2TU in biological fluids has become important.

The electrochemical techniques provide information about the processes taking place when an electric potential is applied to the system under study. Electrochemical techniques are powerful and versatile analytical techniques that offer high sensitivity, accuracy, and precision as well as large linear dynamic range, with relatively low −cost instrumentation. After developing more sensitive pulse methods, the electroanalytical studies are more regularly used in industrial, environmental applications and the drug analysis in their dosage forms and especially in biological samples.

One of the most efficient approaches in pharmaceutical analysis is the use of modern electroanalytical methods, which have the advantage of easy application, high sensitivity, accuracy and selectivity, simplicity and fast (less time-consuming) detection and low cost. When compared with other carbon based electrodes, GPEs have some advantages such as high electrochemical reactivity, commercial availability, good mechanical rigidity, disposability, renewability, low cost and ease of modification [7–9]. Due to their useful and important functions, recently scientists have focused on the usage of these electrodes in many electroanalytical applications [7–12]. The surfaces of GPEs are required to modify with particular electrocatalyst for the fabrication of sensitive sensors [13,14].

In recent years, some polymers have been generally used so that their use is either better suited for a specific application or easier to synthesize in the desired form. For example, poly-

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mers such as polyphenols [15], poly(3-thiophene acetic acid)[16], polypyrrole[17,18], polyaniline[19,20], and others have been used. By taking into consideration of the high adsorption capacity and important properties of GPEs, GPE surface with conductive polymers like polyaniline and polypyrrole, are successfully modified and used for the electrocatalytic oxidation of drugs. The surface of modified electrodes has been characterized by their ability for reacting and binding the target analyte.

Several analytical methods have been employed for the determination of the 2TU [21–26]. In spite of their suitability, some of these methods have employed expensive instruments or materials, and require extra pure solvents which are hazardous. Compared to other electrochemical investigations, conductive polymer film modified electrodes play an important role because of their low background current, wide potential windows, chemical inertness, low cost, and suitability for detection of various organic and biological compounds with low detection limit.

2. Experimental

2.1. Materials and methods

2-thiouracil was obtained from Sigma Aldrich, India. 2TU containing Propylthiouracil Tablet (Macleods pharmaceuticals Ltd., batch no. HPB203B) was purchased from local pharmacy used as pharmaceutical sample. Pencil-lead rods (HB, 0.5 mm in diameter and 6 cm in length) were purchased from a local bookstall. A stock solution of 2TU was freshly prepared in double distilled water. Buffer solutions were prepared as described by Christian and Purdy [27] in the pH range of 3.0–10.4. All other chemicals used were of analytical grade.

2.2. Instrumentation and analytical procedure

Voltammetric measurements were performed with a CHI 630D electrochemical analyzer (CH Instruments Inc., USA). A conventional three-electrode cell was used, consisting an Ag/AgCl (3.0 M KCl) as reference electrode, a platinum wire as a counter electrode, polyaniline (PA) and polypyrrole (PP) modified GPE as working electrodes. All the potentials are given against the Ag/AgCl (3.0 M KCl). pH measurements were performed with an Elico LI 120 pH meter (Elico Ltd.,India).

Staircase voltammetry (SCV) is the simplest pulse voltammetric technique; however, it is probably also one of the most oftenly used for a dynamic electrochemical examination of various compounds. The sequence of pulses in SCV forms a potential staircase. An appropriate potential waveform is illustrated in Fig. S1. Staircase voltammograms are peak-shaped which are same as in linear scan voltammograms. Any way there are some differences between these voltammetries. A linear scan (or cyclic) voltammogram forms a continuous current vs. potential curve, while each staircase voltammogram consists of a number of I − E points. In addition to this, the peak heights obtained under conditions of identical scan rates in linear scan and staircase voltammetries ($v = \Delta E/\Delta t$) may differ considerably.

The parameters for SCV were, initial potential: 0.6 V; final potential: 1.2 V; increase of potential: 0.004 V; sample width: 0.02 s; step period: 0.2; quit time: 2 s; sensitivity: 1×10^{-6} A/V.

2.3. Area of the electrode

The area of the electrode was obtained by the cyclic voltammetric method using1.0 m M $K_3Fe(CN)_6$ as a probe at different scan rates. For a reversible process, Randles – Sevcik Formula (1) was used [28].

$$I_{pa} = (2.69 \times 10^5)n^{3/2}AD_o{}^{1/2}C_o\upsilon^{1/2} \quad (1)$$

where, 'I_{pa}' refers to the anodic peak current, 'n' is the number of electrons transferred, 'A' is the surface area of the electrode, 'D_0' is diffusion coefficient, 'υ' is the scan rate and 'C_0' is the concentration of $K_3Fe(CN)_6$. For 1.0 mM $K_3Fe(CN)_6$ in 0.1 M KCl electrolyte, n = 1, $D_0 = 7.6 \times 10^{-6}$ cm^2s^{-1} [28], then from the slope of the plot of I_{pa} versus $\upsilon^{1/2}$, the surface area of PA/GPE & PP/GPE was calculated and found to be 0.265 & 0.287 cm^2 respectively. These are higher than the area of GPE (0.199 cm^2). This indicates the enhanced electrocatalytic nature of the modified electrodes.

3. Results and discussion

3.1. Electrochemical polymerization of aniline and pyrrole on GPE

The polished GPE was sonicated and finally washed with double distilled water. The prepared GPE was subjected to electropolymerization, using cyclic voltammetry in 0.1 mM each of aniline (Fig. S2(a)) and pyrrole (Fig. S2(b)) monomer separately at the applied potential of −0.6 to 0.8 V with Ag/AgCl (KCl_{sat}) electrode and platinum electrode for 5 cycles. During the process of multiple cycles with increase of cyclic time, the voltammograms gradually decreased. This means that the polyaniline and polypyrrole films were formed and deposited on the surface of GPE. After electrodeposition the electrode was washed with double distilled water and used for the electrochemical experiments.

3.2. Optimization of number of cycles

The response of the PP and PA modified electrodes was found to increase with the increase in the number of cycles (Fig. S3). The highest peak current for the PA and PP modified electrodes was obtained by applying 5 cycles in the electropolymerization. Therefore the optimum number of polymerization cycles was found to be 5.

3.3. Morphological characterization of GPE, PA/GPE, PP/GPE

Atomic force microscopy directly represents the information about the electrode surface. Fig. 1a–c show the surface morphology of GPE, PA/GPE and PP/GPE. As shown in Fig. 1a, the surface of GPE is very smooth and uniform. The AFM pictures of GPE, PA/GPE and PP/GPE show significant difference in the surface morphology, which suggests that the polyaniline and polypyrrole were embedded on the surface of GPE (Fig. 1b & c). The presence of polyaniline and polypyrrole on the surface of the electrode increases the effective surface area and hence increases the rate of electron transfer [29]. The stability and sensitivity of the modified electrode have been confirmed by the performance of PA/GPE and PP/GPE in the electrochemical investigation of $[Fe(CN)_6]^{3-/4-}$ system.

3.4. Electrochemical behavior of $[Fe(CN)_6]^{3-/4-}$ at GPE, PA/GPE and PP/GPE

The redox response of $[Fe(CN)_6]^{3-/4-}$ couple is a valuable and convenient probe to characterize the electrochemical performance of the modified electrode. The performance of PA/GPE and PP/GPE was monitored via the redox behavior of $[Fe(CN)_6]^{3-/4-}$ couple. Fig. S4 represents the cyclic voltammogram obtained at GPE, PA/GPE and PP/GPE in 0.1 M KCl containing 1 mM $K_3[Fe(CN)_6]$. The GPE shows a reversible voltammogram with a peak to peak separation of 57 mV for the $[Fe(CN)_6]^{3-/4-}$ couple (curve c). The redox response