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ORIGINAL PAPER

Electrochemical detection of propofol at the preanodized carbon electrode

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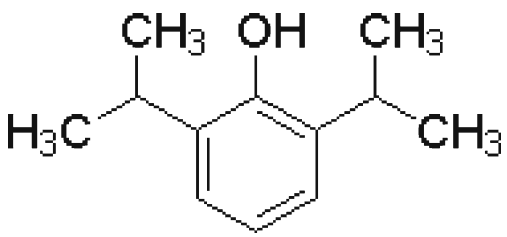
Abstract Preanodized screen printed carbon electrode (SPCE) has been utilized for the detection of propofol. Here the preanodized SPCE possess the specific functional groups which help the detection and determination of propofol. The proposed SPCE shows a clear oxidation peak for the detection of propofol in pH 7.0 phosphate buffer solutions. Interestingly, it shows a well-defined individual oxidation peak for the detection of propofol in the presence interferences (mixture of ascorbic acid, dopamine, and uric acid). This type of pretreated SPCE successfully enhances the electrooxidation current and overcomes the interference effects and clearly exhibits the signals for the propofol detection using cyclic voltammetry and flow injection analysis techniques. The preanodized SPCE shows the electrooxidation signals for the propofol detection in the linear range of 0.09 to 0.90 μM, respectively. Further, the sensitivity of the proposed electrode for the propofol detection is found to be 3.6 μA μM^{-1}.

Keywords Screen printed carbon electrode · Propofol · Dopamine · Ascorbic acid · Uric acid

Introduction

Propofol known as diprivan (2, 6-Bis (Isopropyl)-phenol) is known as hypnotic agent. It has been used for the maintenance of general anesthesia and procedural sedation. Propofol is also employed as veterinary medicine. Propofol is more rapid and effective compared to thiopental (general anesthetic). Due to its appearance as white liquid, it is also called milk of amnesia. Also, propofol is clinically validated as hypnotic agent and available in generic use in more than 50 countries [1–4]. The nonmedical use of propofol is increased around 2009 [5]. The famous pop singer and dancer Michael Jackson died because of the illegal adulteration of mixture of propofol and benzodiazepine drug. His death occurred due to the involvement of propofol as a hypnotic drug [6–10].



Propofol (2, 6-Bis (Isopropyl)-phenol)

Therefore an effective analytical method has to be investigated for the detection and determination of propofol. Previously, various types of analytical techniques have been employed for the detection and determination of propofol. The following techniques have been reported to be employed: For example, the detection and determination of propofol using high performance liquid chromatography (HPLC) [11, 12], supported liquid membrane and liquid chromatography-electrochemical detection [13], HPLC assay of propofol in human and rat plasma and rat tissues using electrochemical detection [14], HPLC assay to detect hydroxylate and conjugate metabolites of propofol in human urine [15], reversed phase HPLC at High pH [16] and HPLC assay of propofol in human and rat plasma and various rat tissues [17] were reported.

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These are the previous literature reports for the detection of propofol. Comparing with these analytical techniques, the electrochemical detection technique is found to be simple and effective for the detection and determination of propofol. Next, the pretreated electrode surface shows excellent catalytic properties for the detection of various chemically important compounds. Number of literature reports has been reported for this type of electrode modification process. For example, oxidized GCE surfaces have been utilized for the various types of electrocatalytic applications [18–22]. Also, in SPCEs, electrocatalytic reduction and determination of dissolved oxygen at a preanodized SPCE modified with palladium nanoparticles [23], electrochemical investigation of glucose sensor fabricated at copper plated SPCEs [24], and simultaneous determination of dopamine (DA), ascorbic acid (AA), and uric acid (UA) detection based oxygen functional and edge plane sites on SPCE have been reported [25].

All these literature surveys clearly show the number of methods for the fabrication of pretreated GCEs and SPCEs and suggest a simple and elegant pathway for the electrode modification process. Also, the preanodization process modifies the electrode surfaces with specific functional groups (carbonyl, carboxyl, and hydroxyl species). Therefore, in this report, we have utilized the preanodization process to modify the SPCE surface with functional groups and employed for the detection of propofol using cyclic voltammetry (CV) and flow injection analysis (FIA). In this report, the surface morphology of preanodized SPCE has been examined by using scanning electron microscopy (SEM) and atomic force microscopy (AFM). The proposed SPCE possesses the capability for the detection and determination of propofol in the reasonable linear ranges using CV and FIA techniques, respectively.

Experimental

Reagents

Propofol, AA, DA, and UA were purchased from Sigma-Aldrich (USA). All other chemicals (Merck) used were of analytical grade (99%). Double distilled deionized water was used to prepare all the solutions. A phosphate buffer solution (PBS) of pH 7.0 was prepared using Na_2HPO_4 (0.05 mol l^{-1}) and NaH_2PO_4 (0.05 mol l^{-1}). Pure nitrogen was passed through all the experimental solutions. Human urine samples have been obtained from a single donor and pretreated several times before the analysis.

Apparatus

All the electrochemical experiments were performed using CHI 1201a potentiostat (CH Instruments, USA). The SPCEs were purchased from Zensor R&D (Taichung, Taiwan). A conventional three-electrode system was used which consists of an Ag/AgCl (saturated KCl) as a reference, bare or preanodized SPCE as working, and platinum wire as counter electrode. Electrochemical impedance studies (EIS) were performed using ZAHNER impedance analyzer (Germany). The morphological characterization has been examined using SEM (Hitachi S-3000H). The AFM images were recorded with multimode scanning probe microscope (Being Nano-Instruments CSPM-4000, China).

Fabrication of preanodized SPCE

The preanodization of SPCE has been done by electrochemical method using cyclic voltammetry. The pretreated GCE was immersed in 0.5 M H_2SO_4, and the potential cycling have been applied between 0 and 2 V at the scan rate of 0.1 V/s for ten cycles (Fig. 1). From the Fig. 1, we can clearly observe the anodic oxidation process of the SPCE surface.

Results and discussion

AFM, SEM, and EIS analysis

The surface morphology of the bare and preanodized SPCEs has been examined using AFM and SEM. Here, the AFM studies could furnish the comprehensive information about the surface morphology of bare and preanodized SPCE surface. The surface morphology of two types of SPCEs has been examined by using the tapping mode (Fig. 2). Here Fig. 2a and b represents the AFM and SEM images of the bare SPCE. In this, the bare SPCE's (Fig. 2a) roughness average (20,425×20,425 nm) is found to be 265 nm, and the root mean square roughness [26] is found

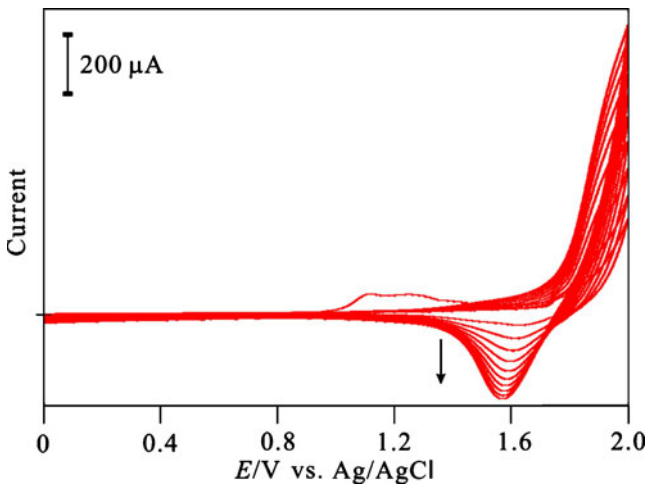

Fig. 1 Consecutive cyclic voltammograms of SPCE anodization process in 0.5 M H_2SO_4 and the potential cycling have been applied between 0 and 2 V at the scan rate of 0.1 V/s for ten cycles

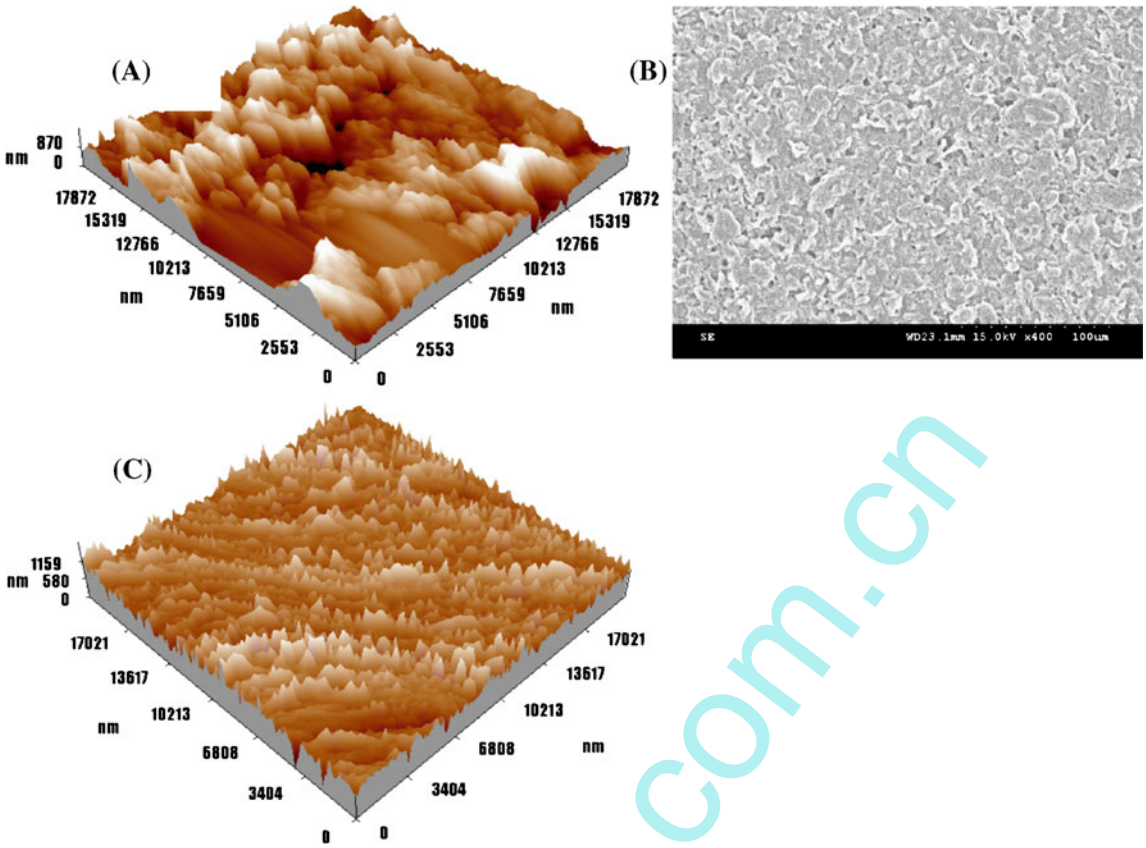

Fig. 2 **a** AFM and **b** SEM images of the bare SPCE and **c** AFM 3D view of preanodized SPCE

as 339 nm. At the same time, for the preanodized SPCE (Fig. 2c) the roughness average is found to be 140 nm. The decrease in the roughness average shows that the anodized SPCE possess the smooth surface nature. By using the combination of skewness and kurtosis values, it is possible to identify the film surfaces which have relatively flat top and deep valleys. The skewness (Rsk) measures the symmetry of variation of the surface about its mean plane [27–29]. The surface skewness for the preanodized SPCE is found to be 0.392. Next, the kurtosis (Rku) is a measure of the unevenness or sharpness of the surface. A surface that is centrally distributed has a kurtosis value greater than 3. For the preanodized SPCE, the kurtosis value was found as 5.17. All these AFM and SEM results clearly depict the surface difference between the bare and preanodized SPCE.

In the next step, the electrochemical activity of bare and preanodized SPCE has been examined using EIS analysis. Impedance spectroscopy is an effective method to probe the features of surface modified electrodes. The complex impedance can be presented as a sum of the real, Z'(ω), and imaginary, Z"(ω), components that originate mainly from the resistance and capacitance of the cell. From the shape of an impedance spectrum, the electron-transfer kinetics and diffusion characteristics can be extracted [30, 31].

Figure 3 shows the Faradaic impedance spectra, presented as Nyquist plots (Z" vs. Z') for the bare and preanodized SPCE. The bare SPCE exhibits almost a straight line (a) that represents the characteristics of diffusion-limited electron-transfer process on the electrode surface. At the same time, the preanodized SPCE shows like a depressed semicircle arc with an interfacial resistance

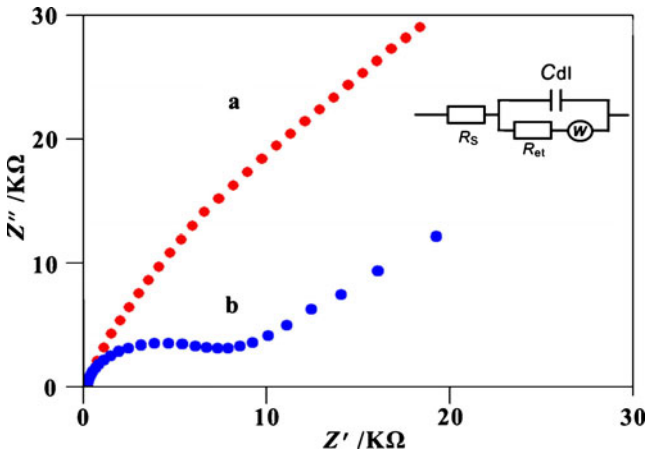

Fig. 3 Electrochemical impedance spectra curves of **a** bare and **b** preanodized SPCE in pH 7.0 PBS containing 5×10^{-3} M $[Fe(CN)_6]^{3-/4-}$

due to the electrostatic repulsion between the charged surface and probe molecule Fe $(CN)_6^{3-/4-}$ (b). This depressed semicircle arc (R_{et}=7.9(Z'/KΩ)) clearly indicates the lower electron transfer resistance (R_{et}) behavior comparing with the bare SPCE. This type of behavior is due to the presence of functional groups and the roughness nature of the anodized SPCE surface [22–25]. Thus, the electron transfer process will become as a slow process on the preanodized SPCE.

Electrocatalytic oxidation of propofol at the preanodized SPCE

Preanodized SPCE has been directly employed for the detection of propofol in pH 7.0 PBS. Fig. 4a curve (a–g) shows the cyclic voltammograms of propofol oxidation at the preanodized SPCE. Here, the anodic oxidation of propofol occurs at the potential range of 0.56 V. At the same time, curve a' displays the propofol oxidation at bare SPCE (0.57 V). Comparing with the preanodized SPCE, the bare SPCE exhibits diminished current response for the propofol oxidation process. Therefore, the proposed preanodized SPCE shows the enhanced anodic current response for the electrooxidation of propofol. Here, the potential shift and the electrooxidation current increase clearly show the good catalytic activity of preanodized SPCE for the detection of propofol. The preanodized SPCE successfully exhibits the detection of propofol in the linear range of 0.09 to 0.90 μM. The sensitivity and the limit of detection for propofol at the preanodized SPCE have been found as 3.6 μA μM^{-1} and 0.08 μM, respectively.

In the next step, interference studies have been examined for the detection of propofol. Cyclic voltammetry has been employed for the selective detection of propofol in the presence of AA (20 μM), DA (10 μM), and UA (50 μM). Here, the preanodized SPCE clearly exhibits the separate oxidation peak for the detection of propofol in the presence of other interfering compounds (AA, DA, and UA). This shows the special property of the preanodized SPCE

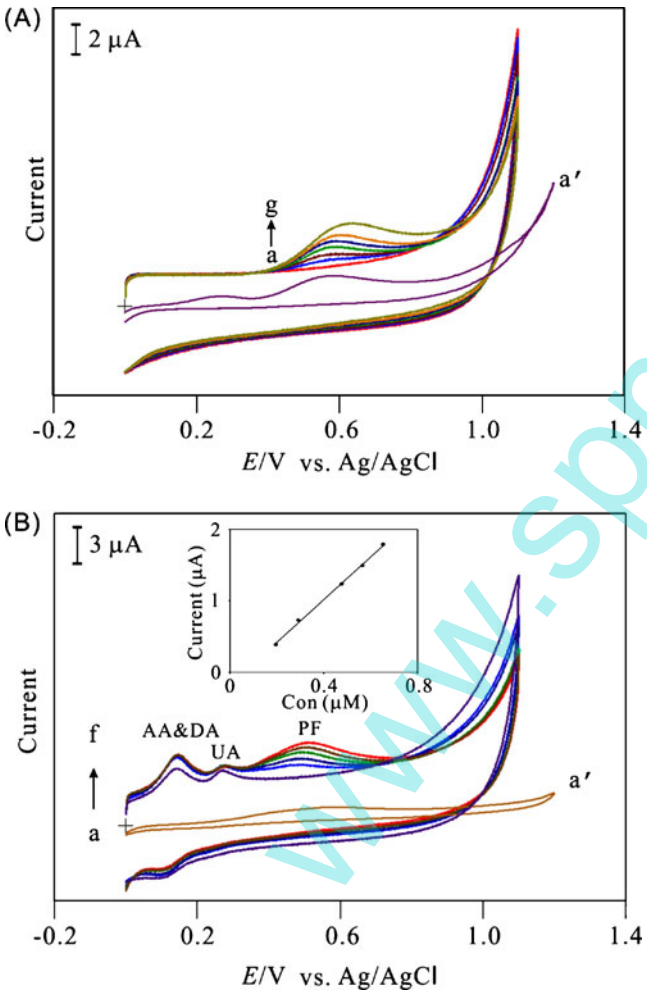

Fig. 4 **a** CVs of propofol electrooxidation at the preanodized SPCE. The propfol concentrations were in the range of *a–g* (0, 0.09, 0.19, 0.38, 0.47, 0.65, and 0.90 μM; in pH 7.0 PBS). *Curve a'* represents the bare SPCE response for the detection of propofol (0.90 μM; scan rate, 0.1 V/s). **b** CV response of preanodized SPCE in the presence of interferences (AA, DA, and UA—20, 10, and 50 μM). Propofol concentration in the range of *a–f* (0, 0.19, 0.29, 0.47, 0.56, and 0.65 μM)

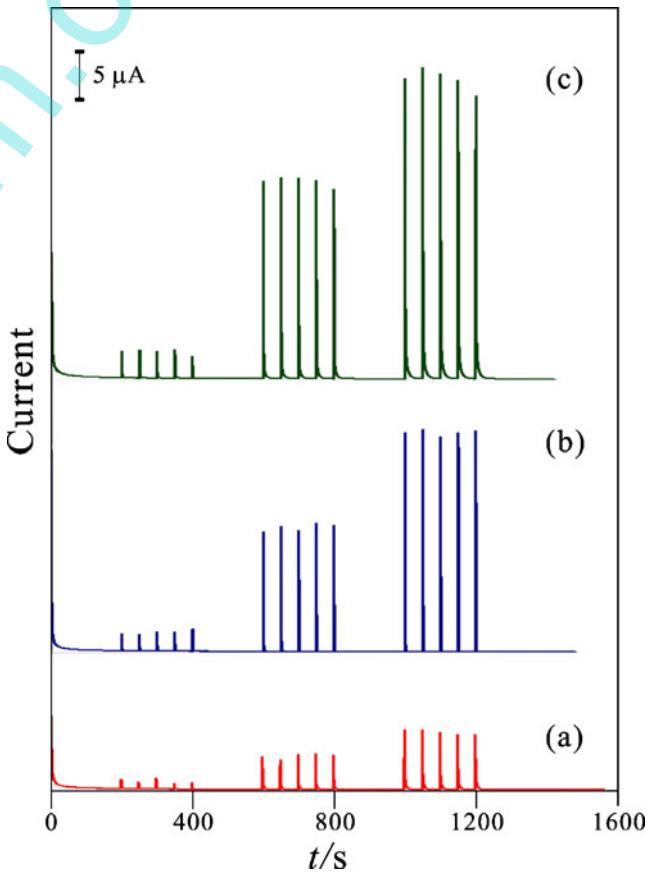

Fig. 5 **a** FIA response of propofol detection (concentration 2, 10, and 30 μM), **b** pretreated urine (2, 20, and 30 μl), and **c** urine and propofol mixture (2, 10 and 30 μM)

(Fig. 4b). This is the due to the presence of the functional groups [22–25] at the preanodized SPCE surface.

Flow injection analysis

The real sample analysis has been examined utilizing the FIA technique. Pretreated urine samples have been employed for the detection of propofol. Figure 5a shows the flow injection response signals for the propofol detection in pH 7.0 PBS. Figure 5b shows the only pretreated urine samples injection signals for the detection of UA, and Fig. 5c exhibits the mixture of pretreated urine and propofol injection signals at the preanodized SPCE. In real sample analysis (urine sample and propofol mixture (Fig. 5c)), the current response is higher than only propofol (Fig. 5a) and only urine (Fig. 5b) analyses. This happens because the presence of UA in the buffer solution automatically enhances the current response for the propofol detection. Here, the flow injection analysis is examined as an auxiliary experiment to support the previous results. In this report, we mainly consider the cyclic voltammetric technique for the detection of propofol. This is because by employing CV, we can easily distinguish the separate electrooxidation signals for the propofol in the presence of interferences (AA, DA, and UA; Fig. 4b).

Table 1 represents comparison chart for the detection of propofol based on various analytical techniques and samples. The Table 1 clearly explicates that most of the reports are based on the chromatography combined with electrochemical detections. Comparing with chromatography-based determinations, the proposed method is found to be simple and direct analysis for the propofol detection process. Here, we did not claim that the proposed method is more sensitive for the detection of propofol. At the same time, comparing with the chromatographic techniques, this method is found to be a direct one, and the selective detection of propofol in the presence of interferences (AA, DA, and UA) is another interesting criterion which could be carried out using this type of modified electrodes.

Conclusion

Here, we report a simple method for the electrochemical detection for the propofol. The preanodized SPCE electrode successfully exhibits the anodic oxidation signals for the detection of propofol in the presence of interferences such as AA, DA, and UA. The preanodized SPCE is found to be much effective for the detection of propofol in physiological pH conditions. Furthermore, the proposed SPCE overcomes the interference effects and effectively shows the oxidation peaks for the detection of propofol in urine samples. Overall, the proposed method is very easy to fabricate and could be applied for the direct detection of propofol in real samples.

Table 1 Comparison table for propofol detection using various methods in various samples

S. No.	Method	Mobile phase (buffer, ratio, pH)	Detection sample	Linear range	Sensitivity	Detection limit	Reference
1	Electrochemical determination and HPLC	0.082 M sodium acetate–phosphate (orthophosphoric acid–ACN (45:55, *v/v*), 4.0)	Serum	100–2,000 ng ml^{-1}	–	80 ng	11
2	Simple and practical HPLC by phenyl column chromatography with electrochemical detection	Methanol–25 mM PBS (1:3, *v/v*, 6.0)	Human blood	500–2,000 ng ml^{-1}	20 ng ml^{-1}	–	12
3	Supported liquid membrane and LC-electrochemical detection	0.05 M sodium phosphate–methanol (1:3, *v/v*, 3.8)	Human urine	–	–	10 ppt	13
4	HPLC–electrochemical detection	50 mM phosphate buffer–methanol (60:40, *v/v*, 2.8)	Human and rat plasma	0.5–100 ng	–	–	14
5	HPLC assay (simple mobile phase and a reversed phase chromatographic column)	ACN–PBS (60:40, *v/v*, 3.8)	Human urine	–	–	–	15
6	Reversed phase HPLC at high pH	Buffer–ACN mixture (60:40, *v/v*, 13.8)	Lab sample	–	–	3×10^{-8} M	16
7	Simple HPLC assay	ACN–water (60:40, *v/v*)	Human plasma and various rat tissues	10 ng ml^{-1}–1 μg ml^{-1}	–	–	17
8	Cyclic voltammetry	PBS (7.0)	Lab sample	0.09–0.9 μM	3.6 μA μM^{-1}	0.08 μM	This work

HPLC high-performance liquid chromatography, *LC* liquid chromatography, *PBS* phosphate buffer solution, *ACN* acetonitrile, *ppt* parts per trillion

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