"Carbon nanotube-CTAB composite film modified sensor for voltammetric determination of antifungal ketoconazole in pharmaceutical and real samples"

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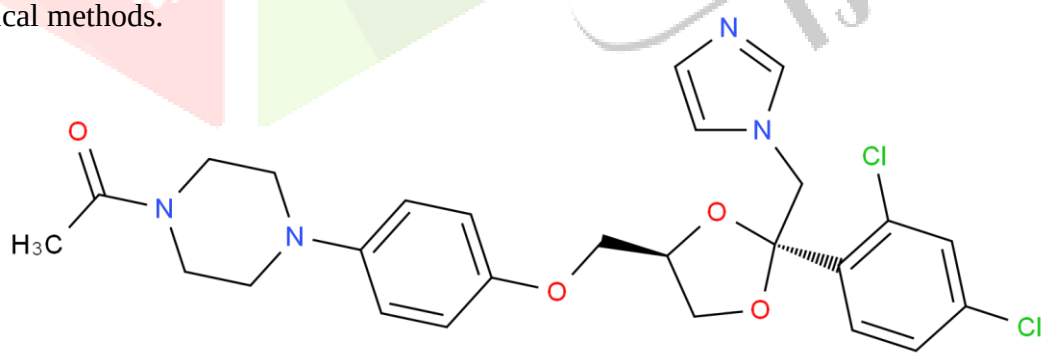
Abstract

An electrochemical sensor was used for the analytical determination of antifungal drug ketoconazole (KTZ) at multi-walled carbon nanotubes with cetyl trimethyl ammonium bromide (CTAB) surfactant composite modified glassy carbon electrode using cyclic voltammetric (CV) and differential pulse voltammetric (DPV) techniques. The modified composite electrodes surface morphology was characterized by using atomic force microscopy (AFM) and scanning electron microscopy (SEM). In the modified nano-composite electrode (MWCNTs-CTAB/GCE) peak current enhances greatly compared with bare GCE and MWCNTs/GCE electrode. The electrochemical oxidation of ketoconazole was studied at pH 7.4 of phosphate buffer (0.2M) solution. Experimental parameters such as pH of supporting electrolyte, scan rate, concentration of KTZ and interferants were investigated. The oxidation process was irreversible and exhibited a diffusion controlled behavior. The current response was found to be directly proportional to the concentration of KTZ in the concentration range of 1.0×10^{-8} M to 1.1×10^{-7} M, with a Limit of Detection (LOD) of 3.48×10^{-9} M. The modified sensor showed excellent electrochemical stability, good selectivity and reproducibility. The proposed method was successfully applied to determination of ketoconazole in pharmaceuticals and real samples. This method can be employed in clinical analysis, quality control and routine determination of drugs in pharmaceutical formulation.

Keywords: Ketoconazole, Voltammetry, Clinical analysis, CTAB, Diffusion controlled, Real samples.

1. Introduction

Ketoconazole (KTZ), *cis*-1-acetyl-4-{4-[2-(2,4-dichlorophenyl)-2-(1*H*-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy} piperazine(Scheme 1), is a most effective when administered orally, for the antifungal drug treatment against a wide variety of superficial and systemic mycoses[1,2]. Ketoconazole is active against specific dermatophytes and yeast, so used in preparation of pharmaceutical medicine like tablets, shampoos and ointment (cream) etc, they are good oral bioavailability and fewer side effects and small fraction of the administered dose was excreted unchanged in the urine. Various methods have been reported for the determination of ketoconazole in drug formulations, among them some including visible spectrophotometry[3,4], UV spectrophotometry[5], spectrofluorimetry[6], thin-layer chromatography[7], and capillary electrophoresis with diode array detection[8,9]. Spectroscopy and chromatography methods involve various lengthy extraction process, time consuming, complex operating process, expensive instruments and strict pre-disposal. The use of electrochemical procedures have been extensively investigated in the determination of biologically important drugs in recent years because of their simplicity, ease of miniaturization, high sensitivity and relatively low cost as compared to other analytical methods.



Scheme 1: Structural formula of ketoconazole

Sensors based on multi-walled carbon nanotubes (MWCNTs) were widely used in various electrochemical applications in the recent years, since they display numerous advantages, such as great electrochemically accessible area, high electrical conductivity, extremely high reactivity

and selectivity, as well as great chemical stability[10]. Furthermore, it was recognized that MWCNTs exhibit improved electric transport properties and electrocatalytic properties and are capable to reduce the over potentials and to improve significantly the currents of redox systems[11-13]. In addition, MWCNTs display high sensitivity and detection capability, and thus, they improve the reaction rate and amplify the stability and reproducibility of electrode's response[14]. Cetyltrimethyl ammonium bromide (CTAB), a cationic surfactant, often used as an absorbent due to the strong hydrophobic interaction between the long alkyl chain of CTAB. In this case, CTAB can be used as electrode modifier for enrichment of MWCNTs on the electrode surface to improve sensitivity. The CTAB could increase the particle growth rate by increasing the reduction rate of MWCNTs and its uniform dispersion increases surface area. The electrostatic force between CTAB and KTZ facilitates reaching of KTZ to the electrode surface faster, and as a consequence, the reaction becomes easier.

Another problem commonly encountered at bare electrode is that they get poisoned by several species and decrease sensitivity and reproducibility. Hence, considerable efforts have been devoted to modify the electrode for enhancing its voltammetric response and analytical performance. In the present work, the dispersion of multiwalled carbon nanotubes in the presence of CTAB surfactant modified glassy carbon electrode was used as suitable sensor for the determination of KTZ. The proposed method was applied to pharmaceutical sample and real samples.

2. Materials and methods

2.1. Reagents and chemicals

Ketoconazole was purchased from Sigma Aldrich limited and multi walled carbon nanotubes (MWCNTs) powder was purchased from Sigma Aldrich. Cetyltrimethyl ammonium bromide was from Merck. A solution of Ketoconazole was prepared by dissolving an appropriate amount

of powdered sample in methanol. Double distilled water was used throughout the work. All other solvents and materials used were of analytical grade.

2.2. Instrumentation and analytical procedure

The electrochemical experiments were performed with a CHI-630D Electrochemical analyzer with a three electrode system. A MWCNT-CTAB/GCE serves as the working electrode, a platinum wire as the auxiliary electrode, and an Ag/AgCl (3.0MKCl) as the reference electrode, respectively. pH measurements were performed with Elico LI120 pH meter (Elico Ltd., India). Experiments were carried out at room temperature.

The parameters for differential pulse voltammetry (DPV) were initial potential: 0.0V; final potential: 1.0; increase potential: 0.004V; amplitude: 0.05V; frequency: 15Hz; with time: 2s; sensitivity: 1×10^{-4} A\V.

2.3. Preparation of modified electrode

To get reproducible results, great care was taken in the electrode pre-treatment. The GCE was pre-treated in two ways: (i) mechanical polishing over a velvet micro-cloth with 0.3 and 0.05m alumina slurry and (ii) electrochemical treatment by applying a potential of 1.25V for 2 s. The electrochemical pre-treatment was done in the same supporting electrolyte solution in which the measurement was carried out. After that 10 µL of solution containing 0.3 g/L MWCNTs and 0.2 g/L CTAB, which was sonicated for 60 min was placed on the GCE surface and then evaporating it in an oven at 50 ^{0}C. The ultrasonication of MWCNTs via CTAB will lead to the dispersion of nanotubes, and fix the surfactants on the surface of MWCNTs[15]. It can be described that the cationic surfactant will make the nanotubes positively charged; these charged MWCNTs are driven towards cathode to form a thin layer at the electrode surface.

Eventually, the coated electrodes (MWCNTs-CTAB/GCE) were immersed in the bicarbonate solution (0.01 M) for 30 min in order to extract the residual surfactants from the surface of

electrode. The modified electrodes were washed with distilled water and dried in room temperature. Fig. 1 shows surface morphology of photography Atomic Force Microscopy (AFM) and Scanning Electron Microscopy (SEM) images of MWCNTs and MWCNTs-CTAB. SEM and AFM are the most appropriate and accurate characterization tools for investigation of surface morphology structure and shape estimation. SEM image showed before the modification were very smooth and after modification were rough which increases surface area and facilitated electrode deposition easily. AFM morphology confirms the more adsorption of MWCNT on the glassy carbon electrode in the presence of the CTAB. Therefore modified electrode surface is rough and shows good conductivity.

(A) (B)

(C) (D)

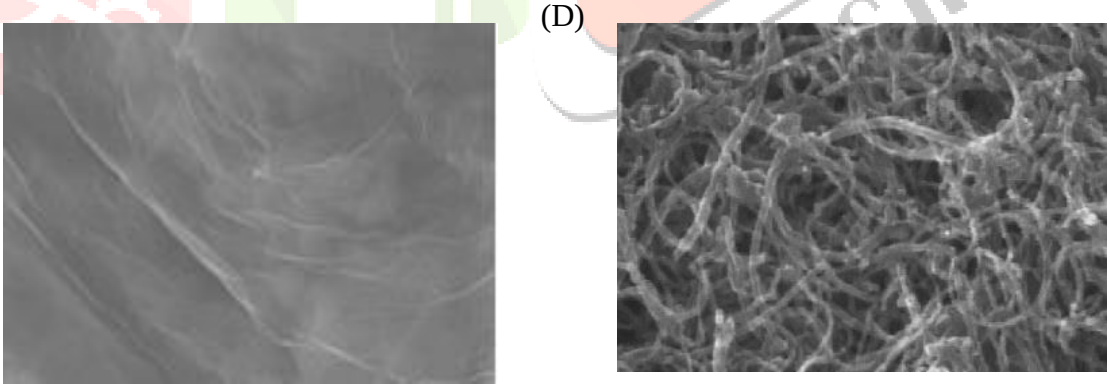


Figure.1 (A) AFM topography of MWCNT. (B) AFM topography of MWCNT with surfactant CTAB (C) SEM topography of MWCNT. (D) SEM topography of MWCNT with surfactant CTAB

2.4. Area of the electrode

The area of the electrode was calculated by the cyclic voltammetric method using 1.0 mM $K_4Fe(CN)_6$ in 0.1 M KCl by recording the current voltage curve at different scan rates. For a reversible process, the following Randles–Sevcik formula can be used [16].

$$I_p = 0.4463 (F^3/RT)^{1/2} n^{3/2} A_0 D_o^{1/2} C_0 v^{1/2}$$

where 'I_p' refers to the anodic peak current, 'n' is the number of electrons transferred, 'A_0' is the surface area of the electrode, 'D_0' is diffusion coefficient, 'v' is the scan rate and 'C_0' is the concentration of $K_3Fe(CN)_6$. For 1.0 mM $K_4Fe(CN)_6$ in 0.1 M KCl electrolyte, n = 1, $D_R = 7.6 \times 10^{-6}$ cm^2 s^{-1}, then from the slope of the plot of I_p versus $v^{1/2}$, the electro active area was calculated. In our experiment the area of electrode was calculated to be 0.118 cm^2. The area of the MWCNTs modified electrode was 0.0749 cm^2 and unmodified glassy carbon electrode was calculated to be 0.0398 cm^2. Electrode surface area of MWCNTs-CTAB/GCE was higher than the MWCNTs/GCE and bare GCE. Hence the greater peak current was observed towards MWCNTs-CTAB/GCE for ketocanazole.

2.5. Preparation of Pharmaceutical Sample

Commercially available Nizoral tablets each containing 200 mg ketocanazole, were weighed accurately made a homogeneous fine powder in a mortar. An amount equal to the calculated average tablet mass was transferred to a 25ml flask, and dissolve by using methanol. The mixture was sonicated for 15 min to achieve complete solubility and there after filtered the solution to 50ml calibrated flask diluted up to the mark use for further analysis.

Nizoral shampoo and Keto-B cream each containing 2% ketocanazole were dissolved each in 10ml of 0.1 M HCL and filtered the solutions, collect the filtrate and transferred the solutions in to separate 50 ml calibrated flask diluted by using millipore water collected a stock solution for further study. The differential pulse voltammograms (DPV) were recorded between

0.20V and 0.90 V after open-circuit accumulation for 10 s with constant stirring. The oxidation peak current of KTZ was measured. The parameters for DPV were pulse increment of 0.004 V, pulse amplitude of 0.005 V, pulse width of 0.2 s, sample width of 0.02s, pulse period of 0.5 s. To study the accuracy of the proposed method and to check the interferences from common excipients used in pharmaceutical preparation was examined, recovery experiments were carried out. The concentration of KTZ was calculated using standard addition method.

2.6. Plasma sample preparation

Human plasma sample was prepared as described in the earlier report of our work [17]. Human blood samples were collected in dry and evacuated tubes (which contained saline and sodium citrate solution) from a healthy volunteer. The samples were handled at room temperature and were centrifuged for 10 min at 1500 rpm for the separation of plasma within 1 h of collection. The samples were then transferred to polypropylene tubes and stored at -20 ^{0}C until analysis. The plasma samples, 0.2 mL, were deprotonised with 2 mL of methanol. After vortexing for 15 min, the mixture was then centrifuged for 15 min at 6000 rpm, and supernatants were collected.

3. Results and discussion

3.1. Electrocatalytic response of KTZ at the MWCNT-CTAB modified glassy carbon electrode

A cyclic voltammetry was used to investigate the electrochemical behavior of ketocanazole on a MWCNTs-CTAB/GCE in the phosphate buffer solution (0.2 M, pH 7.4) at a scan rate of 50 mV s^{-1}. Voltammetric responces of KTZ at different electrodes like GCE, MWCNTs-GCE and MWCNTs-CTAB/GCE modified electrode are shown in Fig. 2. Compared to all three electrodes MWCNTs-CTAB/GCE gives excellent surface area and sharp oxidation peak which indicate that modified electrode has good catalytic activity for oxidation of KTZ. On the reverse scan, no corresponding reduction peak was observed indicating that the electrode process of ketoconazole is an irreversible one.

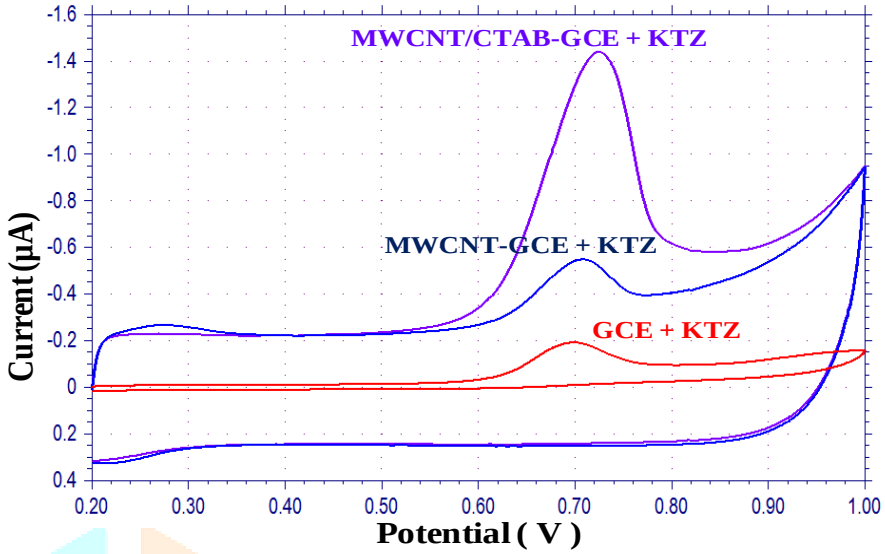


Figure 2. Cyclic voltammogramm obtained for 1.0 mM KTZ at pH 7.0 phosphate buffer (0.2 M) solution at different electrodes GCE, MWCNT-GCE and MWCNT/CTAB-GCE Scan rate 50mVs^{-1} respectively.

3.2. Effect of pH

The electrochemical response of KTZ at MWCNT-CTAB/GCE was generally dependent on pH. The voltammograms of KTZ were recorded at buffer solutions of different pH from pH 3.0 –9.2 by cyclic voltammetric method. Fig. 3(A) demonstrates the pH dependence of KTZ at MWCNT-CTAB/GCE at scan rate of 50 mV s^{-1}. Peak potentials were shifted to less positive side with increasing in the pH values. The peak potential of KTZ shifted from +0.78 mV to +0.66 mV with increase in the pH 3.0 –9.2. The potential-pH diagram was constructed by plotting the graph of E_p vs. pH of the solution (Fig. 3(B)). There was a linear relationship between the peak potential and the pH value as follows.

$$E_p\,(V) = 0.874 - 0.024\ pH \qquad (r = 0.975)$$

The graph shows good linearity with a slope of 24 mV/pH this behavior is nearly equal to theoretical value 30 mV/pH obeyed the Nernst equation for unequal number of electron and

proton transfer reaction [18-20]. From the graph of I_p vs. pH, maximum current was obtained at pH 7.4 (Fig. 3(c)) and for further studies, pH 7.4 was selected for KTZ determination.

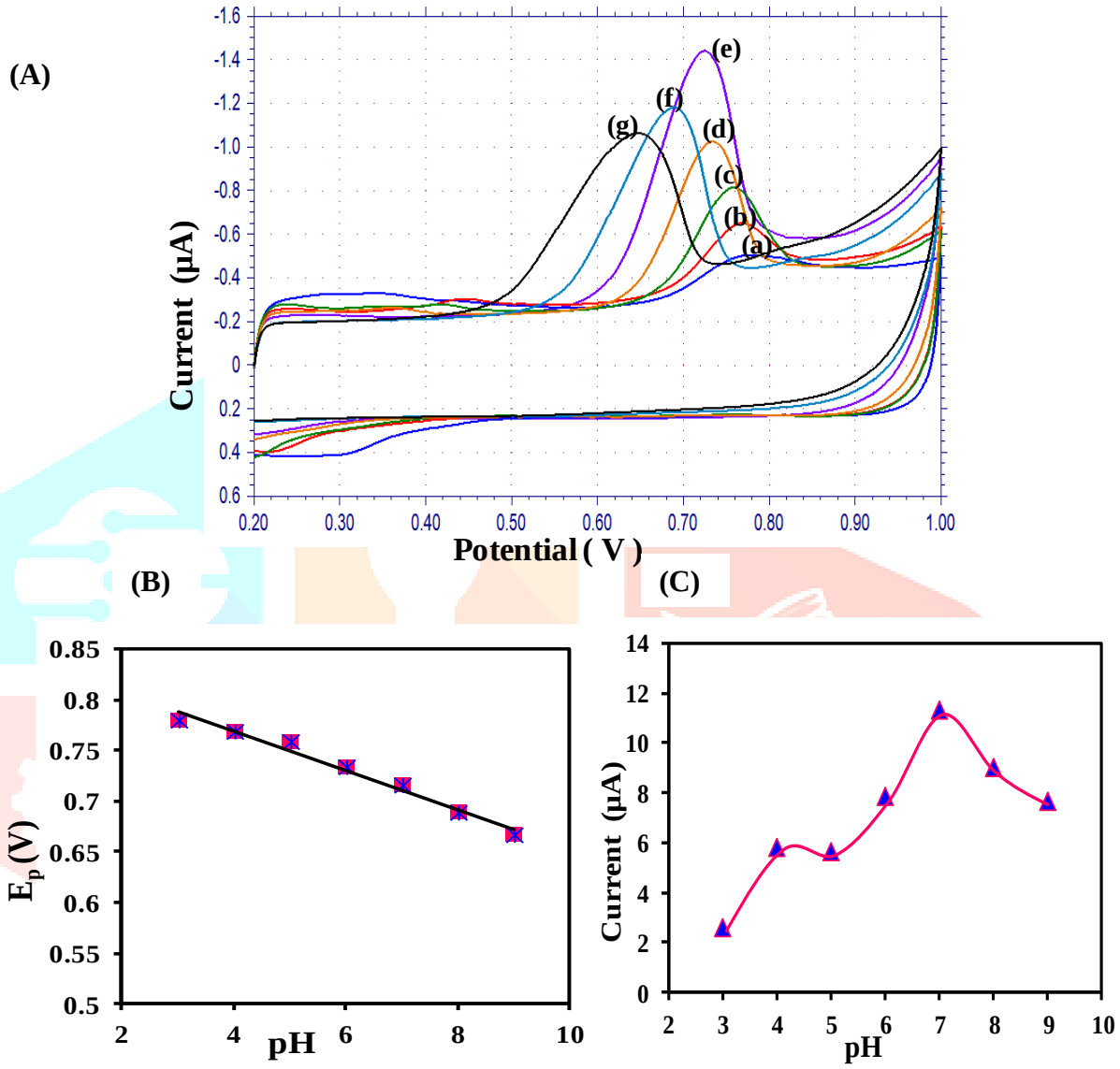


Fig. 3 (A). Cyclic voltammograms of 1.0 mM KTZ at MWCNT/CTAB-GCE different pH (a) 3.0, (b) 4.2, (c) 5.0, (d) 6.0, (e) 7.0, (f) 8.0, (g) 9.2. (B). Influence of pH on the peak potential of 1.0 mM ketoconazole on MWCNT/CTAB-GCE at a scan rate of 50mV s^{-1} in phosphate buffer. (C).Variation of peak current with pH of 1.0mM ketoconazole MWCNT/CTAB-GCE at scan rate of 50 mV s^{-1}

3.3. Effect scan rate

The effect of scan rate on the electro-oxidation of KTZ at the MWCNT-CTAB/GCE was investigated by cyclic voltammetry to acquire information about electrochemical mechanism

from the relationship between peak current and scan rate. The cyclic voltammograms of 0.1 mM KTZ at MWCNT-CTAB/GCE (Fig. 4(A)) were recorded at different scan rates from 0.025 to 0.300 V s^{-1}, as well.

Figure 4. (A). Cyclic voltammograms of 1.0 mM ketoconazole at different scan rates (**a to l** : 25 to 300 mV s^{-1} respectively) in 0.2 M phosphate buffer solution

A linear relationship was observed between log I_{pa} and log *v*, (Figure 4(B)) corresponding to the following equation:

$$\log I_p(\mu A) = 0.367 \log v\ (V\ s^{-1}) + 0.975;\ (r = 0.997)$$

The slope value of 0.367 was comparable with the theoretically expected value of 0.5 for typical diffusion controlled[21]. The peak potential shifted to more positive values on increasing the scan rate. The linear relationship between peak potential and logarithm of scan rate (Fig. 4(C)), which confirms the irreversibility of the oxidation process and expressed as equation E_p (V) = 0.113 log *v* (V s^{-1}) + 0.839; (r = 0.974). According to Laviron[22], E_p is defined by the following equation;

$$E_p = E^{0'} + \left(\frac{2.303RT}{\alpha nF}\right)\log\left(\frac{RTk^0}{\alpha nF}\right) + \left(\frac{2.303RT}{\alpha nF}\right)\log v$$

where 'α' is the transfer coefficient, 'k^0' the standard heterogeneous rate constant of the reaction, 'n' the number of electrons transferred, '*v*' the scan rate and '$E^{0'}$' is the formal redox potential.

T = 298 K, R= 8.314 J $K^{-1}mol^{-1}$, and F=96480 C mol^{-1}. Thus the value of "αn" can be easily calculated from the slope of E_p versus log *v*. the slope value is 0.839.

According to Bard and Faulkner[23], α can be expressed as

$$\alpha = \frac{47.7}{E_p - E_{p/2}}\ mV$$

where $E_{p/2}$ is the potential when the current is at half the peak value. For an irreversible electrode process the transfer coefficient "α" value calculated to be 0.48 and the value of "αn" is 0.749. Thus, the number of electron transferred in the oxidation reaction of KTZ at nano-composite

electrode was found to be 1.67 ≈ 2.0. The k^0 was calculated from the intercept of E_p vs. log *v*. $E^{0'}$ was obtained from the intercept of E_p vs. *v* curve by extrapolating to the vertical axis at *v* = 0 [20]. From the intercept values of laviron plot (0.839) and E_p vs. *v* (0.673) the k^0 value was calculated to be 3.95×10^2 s^{-1}.

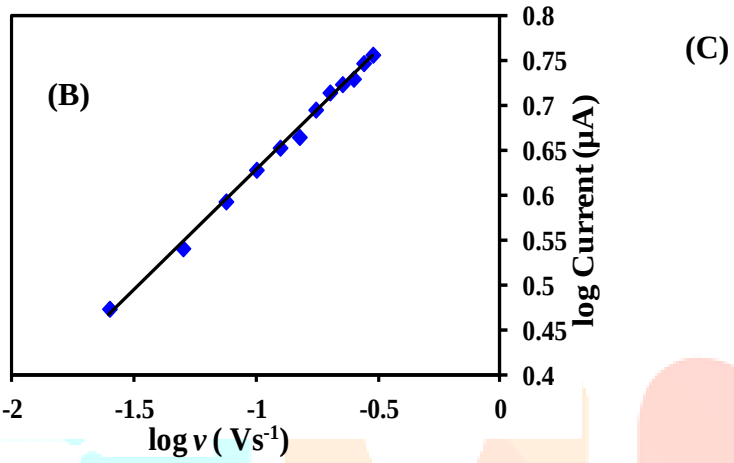


Figure 4. (B). Relationship between the log peak current versus log scan rate. (C). Relationship between the peak potential versus logarithm of scan rate

3.5. Calibration determination

Under the optimized experimental conditions, the quantitative analysis of KTZ was carried out by the fabricated sensor. Since a large capacitive current existed in CV measurements, the differential pulse voltammetry (DPV) was applied in this assay because its charging current contribution to the background current is quite low. Fig. 5(A) shows the dependence of the DPV oxidation peaks on the concentrations of KTZ. It is found that with the increase of the KTZ concentrations, the DPV oxidation signals enhance gradually, and an excellent linearity Fig. 5(B) is observed over a wide concentration range from 1.0×10^{-8} M to 1.1×10^{-7}M, linearity equation.

I_p (10^{-7}A) = 1.258 [KTZ] (10^{-7}M) + 0.248 (r=0.908)

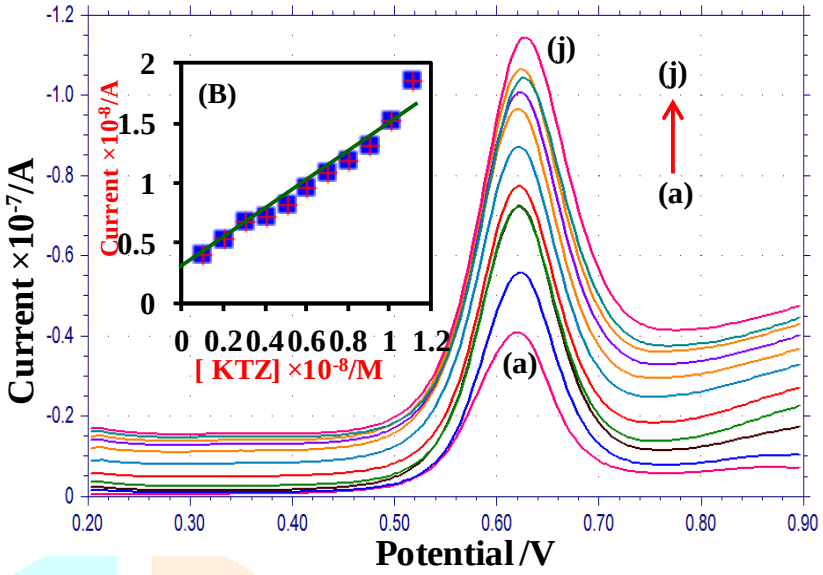


Figure 5. (A) Differential-pulse voltammograms with increasing concentration of KTZ from 1.0×10^{-8} M to 1.1×10^{-7} M at pH 7.4 of phosphate buffer solution on a MWCNTs/CTAB-GCE. (B). Voltammetric peak current versus concentration of ketoconazole

The detection limit (LOD) was estimated to be 3.48×10^{-9} M and the limit of quantification (LOQ) was found to be 1.15×10^{-8} M respectively. The LOD and LOQ were calculated using the following equations;

$$LOD = 3s/m \qquad LOQ = 10s/m$$

where, 's' is the standard deviation of the intercept (five runs) and 'm' is the slope of the calibration curve. Referring to the analytical performances of some recently published reports[24-26] (Table 1), it is found that the obtained detection limit in this work is lower than other modified electrodes, which is likely related that MWCNT-CTAB have high electro catalytic and surface area effects. Compared with the electrode modified with the other materials our developed method shows the lower detection limit and the wider kinetic range, suggesting that the developed sensor in this work can be served as a promising platform for the sensitive detection of KTZ in low concentration.

Table 1. The detection limits for Ketoconazole using different analytical methods are tabulated below

	Analytical methods	Detection limits	Reference no.
1	Voltammetric behavior of ketoconazole and its determination in cosmetic preparation using a b-cyclodextrin modified glassy carbon electrode	**1.05×10^{-7} M**	**[23]**
2	Electrochemical Behavior and Determination of Ketoconazole from Pharmaceutical Preparations	**5.0×10^{-6} M**	**[24]**
3	Electrooxidation of Some Antifungal Agents and Their Square-Wave Voltammetric Determination in Cosmetics and Pharmaceutics	**7.47×10^{-8} M**	**[25]**
4	Carbon nanotube-CTAB composite film modified sensor for voltammetric determination of antifungal ketoconazole in pharmaceutical and real samples	**3.48×10^{-9} M**	**Present**

To investigate the repeatability of the MWCNT-CTAB electrode, electrochemical oxidation of ketocanazole at the same conditions were performed by using different electrodes. The results showed that an acceptable repeatability with a RSD of 3.77% was obtained. The results indicate that the MWCNT-CTAB electrode has a good stability and reproducible.

3.6. Determination of KTZ in pharmaceutical preparations and recovery test

The proposed method was validated for the determination of KTZ in pharmaceutical preparations in Nizrol® tablets (200 mg per tablet), Keto-B cream and Nizrol® shampoo as real samples by applying DPV using the standard addition method. Nizrol® tablets were weighed and ground to a homogeneous fine powder in a mortar. A portion equivalent to a stock solution of a concentration of about 0.01 M was accurately weighed and transferred into a 50 mL calibrated flask and completed to the volume with dilute HCL. The contents of the flask were sonicated for 15 min to affect complete dissolution. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant liquor and diluting them with the phosphate buffer solution. Each solution was transferred to the voltammetric cell and analyzed by standard addition

method. The differential pulse voltammograms were recorded between 0.0 and 0.9 V. The oxidation peak current of KTZ was measured at scan rate of 50 mV s^{-1}. The concentration of KTZ was calculated using the standard addition method. The results are in good agreement with the content marked in the label (Table 2).

Table 2. Analysis of ketoconazole pharmaceuticals and recovery studies.

	Nizoral Tablet	Nizoral Shampoo	Keto-B Cream
Labeled claim (mg)	200	2%	2%
Amount found (mg)[a]	198.8	1.92%	1.95%
Recovery (%)	97.4	95.5	96.6
RSD (%)	1.64	2.86	3.47
Bias (%)	-1.7	-3.8	-0.9
Added (mg)	2	1	1
Amount found (mg)[a]	1.95	0.96	0.98
Recovery (%)	97.5	98.9	98.8
RSD (%	0.356	1.3	1.10
Bias (%)	-1.43	-2.18	-3.02

[a]Average five determinations

The applicability of proposed method in commercially available ketoconazole containing Keto-B cream by using differential pulse voltammetry was subsequently recorded employing the optimized conditions. The procedure for the pharmaceutical analysis was followed as described in the experimental section. To quantify the unknown amount of ketocanazole in solutions, the concentration of the pharmaceutical formulations was determined with the help of calibration curve. The obtained results are in good agreement with the content marked in the label. Table 2 shows that the content values determined by the proposed method for the commercial samples.

3.7. Interference study

For the possible analytical application of the proposed method, the effect of some common excipients used in pharmaceutical preparation was examined. The tolerance limit was defined as the maximum concentration of the interfering substance that caused an error less than ±5% for

determination of KTZ. The effects of these excipients on the voltammetric response was carried by analyzing sample solutions containing a fixed amount of KTZ (1.0 µM) spiked with 100-fold excess amount of each excipient under the same experimental conditions. The potential interference for the determination of KTZ was also studied. Under the optimized conditions, the oxidation peak of KTZ was individually measured in the presence of different concentrations of the common interferents, and then the change of peak current was checked. It is found that glucose, oxalic acid, sucrose, tartaric acid, lactose, starch, citric acid, dextrose, gum acacia, ascorbic acid, and uric acid almost have no influence on the detection of KTZ the experimental results showed (Table. 3), revealing that this sensor has good selectivity for KTZ determination hence it is specific.

Table 3. Influence of interferences on voltammetric signals of KTZ

Interference + KTZ (µM)	Potential (V)	(%) Signal Change
KTZ	**0.742**	
KTZ + Glucose	0.763	-2.830
KTZ + Oxalic acid	0.766	-3.234
KTZ + Sucrose	0.737	0.673
KTZ + Tartaric acid	0.769	-3.638
KTZ + Lactose	0.751	-1.212
KTZ + Starch	0.744	-0.269
KTZ + Citric acid	0.717	3.369
KTZ + Dextrose	0.751	-1.212
KTZ + Gum acacia	0.735	0.943
KTZ + Ascarbic acid	0.723	2.560
KTZ + Uric acid	0.769	-3.638

3.8. Determination of Ketocanazole in Urine sample and human serum plasma

The developed differential pulse voltammetric method for the Ketocanazole determination was applied to urine samples. The recoveries from urine were measured by spiking drug free urine with known amounts of Ketocanazole. The urine samples were diluted 100 times with the phosphate buffer solution before analysis without further pretreatments. A quantitative analysis can be carried out by adding the standard solution of Ketocanazole into the detection system of urine samples and the peak linearly increased. The calibration graph was used for the determination of spiked Ketocanazole in urine samples with a recovery range of 99.2 to 100.2 %. The results of three urine samples obtained are listed in Table 4.

The determination of Ketocanazole in a human serum plasma sample was investigated. Methanol was added to plasma sample and then centrifuged. Sample was diluted with PBS pH=7.0 and spiked with solutions of Ketocanazole by standard addition method. Differential pulse voltammetric method was applied to the analysis of samples. The recovery determined was in the range from 99.6 to 100.8 %, and the RSDs are listed in Table 4. Thus, satisfactory recoveries of the analyte from the real samples make the developed method applicable in clinical analysis.

Table 4. The determination of KTZ in spiked human urine and blood plasma samples

Added	Found(x 10^{-7})[a]	%recovery	Bias(%)	SD(%)	RSD(%)
Urine Samples					
1	0.998	99.8	-0.2	0.009	0.974
3	2.977	99.2	-0.76	0.11	3.727
5	5.012	100.2	0.24	0.045	0.912
7	6.983	99.7	-0.22	0.075	1.076
Plasma Samples					
2	2.016	100.8	0.793	0.029	1.43
4	4.017	100.4	0.423	0.045	1.13

6	5.978	99.6	-0.200	0.078	1.3
8	7.996	99.9	-0.050	0.087	1.09

[a]Average five determinations

3.9. Stability and repeatability of electrode

To investigate the repeatability of the MWCNT-CTAB electrode, electrochemical oxidation of ketocanazole at the same conditions were performed by using different electrodes. The results showed that an acceptable repeatability with a RSD of 3.77% was obtained. The results indicate that the pretreated electrode has a good stability and reproducible.

4. Conclusion

A new method is described for the determination of Ketoconazole which is simple, fast and excellent sensitive with a low cost analysis. A comparison of the voltammetric response of Ketoconazole at bare GCE, MWCNTs modified GCE and MWCNTs-CTAB composite modified GCE clearly revealed that MWCNT in presence of CTAB acts as a better surface modifier in comparison to MWCNTs. Such a deposition imparts different effective surface areas to electrodes. The quantitative evaluation of the KTZ was carried out in the range of 1.0×10^{-8} –1.1×10^{-7} M with a low LOD of 3.48×10^{-9} M at MWCNTs-CTAB modified GCE. To the best of our knowledge, this limit of detection is the lowest value reported for Ketoconazole using modified electrochemical techniques. The MWCNT-CTAB modified GCE exhibited a stable and reproducible response for Ketoconazole determination without any influence of physiologically common interferents. The usefulness of the method was demonstrated by applying it to the analysis of pharmaceutical preparations and human urine and plasma samples. Thus, the proposed method using differential pulse voltammetry is of beneficial use in analytical applications.

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