

Electrochemical Sensor Based on Nanocomposite of Multi-Walled Carbon Nano-Tubes (MWCNTs)/TiO₂/Carbon Ionic Liquid Electrode Analysis of Acetaminophen in Pharmaceutical Formulations

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ABSTRACT: This study aimed at preparing a Carbon Ionic Liquid Electrode (CILE) modified with a new composite of Multi-Walled Carbon Nano-Tubes (MWCNTs) and TiO₂ nanoparticles for AC determination. The proposed electrode was made of a Carbon Paste Electrode (CPE) modified with TiO₂ Nano-Particle (NP)-decorated MWCNTs and a binder of IL 1-hexyl-pyridinium hexafluorophosphate (HPFP) (MWCNT/TiO₂/CILE). The nanocomposite structure characterization was done via X-ray Energy-Dispersive Spectroscopy (EDS) and Field-Emission Scanning Electron Microscopy (FESEM). The electrochemical behavior of Ac was investigated via the Cyclic Voltammetry (CV) technique at the MWCNT/TiO₂/CILE. The MWCNT/TiO₂/CILE was applied for Ac determination by Square-Wave Voltammetry (SWV) technique in real samples. The excellent electrocatalytic activity of the proposed nanocomposite leading to Ac electrochemical oxidation in phosphate buffer solution (pH 6.0) was evidenced. The results of Square-Wave Voltammetry (SWV) revealed a wide linear range of 0.01-30 μM and the detection limits of 0.003 μM for the modified electrode under optimal conditions. This electrode was successfully employed to detect Ac concentrations in plasma and tablet samples with good repeatability and reproducibility.

KEY WORDS: Acetaminophen; TiO₂ nanoparticles; Electrochemical; Carbon Ionic Liquid Electrode (CILE); Determination.

INTRODUCTION

Acetaminophen (N-acetyl-p-aminophenol or paracetamol) (Ac) is one of the most extensively used drugs in the world for relieving such pains as cancer pain and neuralgia leading to a headache, backache, toothache, etc. Nevertheless, its overdoses may lead to the accumulation of toxic metabolites seriously causing fatal hepatotoxicity and nephrotoxicity, as well as pancreatic inflammation, liver

disorders and skin rashes [1]. Thus, it is highly important to develop a simple and accurate method for its detection.

To the best of our knowledge, the few methods reported for Ac determination in biological fluids and pharmaceutical formulations include High-Performance Liquid Chromatography (HPLC) [2], High-Performance Thin-Layer Chromatography (HPTLC) [2], Reversed-Phase

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High-Performance Liquid Chromatographic/Ultra-Violet (RP-HPLC/UV) detection [3], Capillary Electrophoresis (CE) [4], UV-Vis spectrophotometry [5], and electrochemical methods [6-7].

However, the mentioned techniques often suffer from high-cost equipment and laborious time-consuming procedures, including pre-treatment processes. Alternatively, electrochemical methods, especially those incorporating modified electrodes, provide attractively simple and less time-consuming techniques of high selectivities and sensitivities without the need for pre-treatments [8-13]. Hence, these methods can be utilized as better alternatives for Ac determination. It is worth mentioning that CILE was first fabricated by Maleki et al. as a highly efficient carbon composite electrode in 2006 [14]. The so-called homogeneous structure serving as a thick binder in CPEs was provided by ILs [15]. Due to their specific characteristics, such as wide electrochemical potential, high ionic conductivity, polarity, and catalytic activity, and good solubility and antifouling ability, ILs can be used as modifiers in electrochemical sensors [16-17]. In this research, the CILE preparation was done by using 1-hexylpyridinium hexafluorophosphate (HPPF₆) IL instead of oil as a binder together with a modifier based on the traditional CPE.

Due to their unique properties, such as a large surface area, high electrical conductivity, and excellent electrocatalytic activity, CNTs have been utilized for electrode modification [18-20]. Moreover, CNT-based nanocomposites have recently attracted great attention for incorporating synergistic components (CNT/IL hybrids) in the structures of electrochemical sensors [21-27].

On the other hand, metal oxide nanomaterials, especially TiO₂, are the most attractive inorganic materials that have been applied in the preparation of chemically modified electrodes due to their excellent properties, such as a large surface area, thermal stability, low toxicity, and good biocompatibility [28-30]. To electrochemically analyze important biological compounds, electrodes have been modified by hybridizing TiO₂ NPs with some compounds like Carbon Nano-Tubes (CNTs) in ILs [31,32] so as to promote their response repeatabilities by providing more active sites at their surfaces. Also, the combined effect of CNTs and TiO₂ nanoparticles is a strategy to reach high electrochemical responses for electrochemical sensors and biosensors due to the optimization of biocompatibility,

aspect ratio, and electrical conductivity [33].

The present study reports electrochemical behavior and determination of Ac by MWCNT/TiO₂/CILE nanocomposite modified. Due to the synergistic effects of MWCNT and TiO₂ and their interaction with the IL, the electrochemical responses of Ac were greatly enhanced. The results demonstrated the significant elevation of the oxidative peak current of Ac induced by the mentioned nanocomposite, thus leading to good stability and reproducibility.

EXPERIMENTAL SECTION

Chemical reagents

MWCNTs with a purity of >95%, outer diameters of 5-10 nm, and tube lengths of ~30 μm were obtained from Shenzhen Nanotech Port Co., Ltd. (Shenzhen, China). Pure graphite powder and HPFP were purchased from Merck.

Ac was kindly provided by Aboureyhan Pharmaceutical Company (Tehran, Iran). The other chemicals purchased from Merck Company were of analytical reagent grade. By dissolving an optimally precise amount of Ac, a stock solution of 1.0×10^{-2} mol/L was freshly prepared. Other fresh solutions were prepared by diluting the optimal stock solution with distilled water. Each experiment was conducted by applying 0.1 M phosphate buffer solutions with various pH values at 25 ± 1 °C.

The drug-free plasma samples belonging to healthy male volunteers were collected from the Blood Transfusion Organization (Khorramabad, Iran) and stored frozen until assayed.

Instrumentation

An Autolab PGSTAT 204 potentiostat/ galvanostat (Eco Chemie, Utrecht, and the Netherlands) was employed to perform the electrochemical experiments using NOVA 1.11 software. The reference electrode consisting of an Ag/AgCl electrode (KCl 3M) was inserted inside a 3-electrode cell holder. A Pt-wire and the MWCNT/TiO₂/CILE nanocomposite were used as the counter and working electrodes, respectively. The Ag/AgCl electrode and Pt-wire were obtained from Metrohm. For pH measurements, a pH/mV meter (Metrohm, 827 pH lab, Switzerland) was utilized.

SEM was employed for studying the nanocomposite structure and morphology. Energy-dispersive X-ray spectra were recorded using HORIBA EMAX X-ACT (Model 51-ADD0009).

Preparation of TiO₂ NPs

TiO₂ NPs were prepared by applying the sol-gel method described in the literature [34] as follows: First, 35 mL of titanium isopropoxide solution was added to 80 mL of acetic acid and homogenized for 30 min under stirring conditions. Next, 160 mL of deionized water was added dropwise to the solution for 3 h under stirring conditions. The sol-gel was left in darkness for 12 h and then dried. Finally, the dried TiO₂ NPs were calcined at 90°C for 4 h.

Preparation of the MWCNT/TiO₂/CILE-modified electrode

The MWCNTs were refluxed in a mixture of concentrated H₂SO₄/HNO₃ (3:1, v/v) for 15 h, rinsed with twice-distilled water, and dried at room temperature to remove any impurities in the nanotubes and improve electron transfer.

Graphite powder and paraffin were mixed at the 70/30 (w/w) blend ratio in a mortar and pestle to prepare the unmodified CPE. The resulting paste was firmly pressed into the cavity (1.8-mm i.d.) of a Teflon cylinder. The electrical contact was made with a copper wire.

90% graphite powder was mixed with 10% IL to prepare a CILE. The electrode was heated in an oven up to a temperature of higher than IL melting point (m.p. ~65°C) for 2 min before use so as to obtain a better homogenous composite and reduce the background current [33-34]. 10% MWCNT was mixed with 10% IL and 80% graphite powder to prepare the MWCNT/CILE-modified electrode. Also, 25% TiO₂ was mixed with 10% IL and 65% graphite powder to prepare the TiO₂/CILE-modified electrode. Finally, MWCNT/TiO₂/CILE nanocomposite electrode was prepared by mixing 10% MWCNT, 25% TiO₂, 10% IL, and 55% graphite powder together.

Preparation of real samples

The treatment of 5.0 mL of the plasma samples with 10 mL of methanol was begun to provide protein precipitation and elimination. The supernatant obtained by vortexing the mixture for 2 more minutes was centrifuged at 3000 rpm for 8 min. It was then evaporated under a nitrogen

stream after being transferred to a small flask. Ultimately, the dry residue dilution (5.0 mL) was conducted in a phosphate buffer solution (55.0 mL; pH 6.0) to be then analyzed in the voltammetric cell with no further pretreatments. Acetaminophen was determined in the samples using the standard addition method.

Consultations were established by the calibration equations of the calibration curve method. Ten 325 mg tablets of Ac were ground in a mortar after weighing them. A 100-mL calibrated flask was utilized to dissolve sufficient amounts of the weighed powder. The Ac samples were finally analyzed by using the standard addition method.

RESULTS AND DISCUSSION

The structural characterization of MWCNT/TiO₂/CILE

The SEM images of CILE (A), MWCNT/CILE (B), TiO₂/CILE (C), and MWCNT/TiO₂/CILE (D) were recorded as displayed in Fig. 1. As portrayed in Fig. 1A, the CILE has a flat surface due to the IL high viscosity in the carbon paste binding the carbon powders together.

Figs. 1B and 1C represent MWCNT and TiO₂ NPS spreading well on the CILE surface. As for the MWCNT/TiO₂/CILE composite (Fig. 1D), it can be seen that TiO₂ and MWCNT have been well dispersed on the CILE surface and some have entered into its structure, indicating the complete and uniform mixture of TiO₂ and MWCNT with the CILE to form a homogeneously hybrid composite. Also, Fig. 1E illustrates a histogram of the particle size distribution of nanoparticles for Fig. 1C with an average size of about 34 nm.

Fig. 2 shows the EDX spectra of the composite for MWCNT/TiO₂/CILE. The results of the EDX spectra also confirmed the presence of Ti, N, O, and C on the nanocomposite (Fig. 2).

The electrocatalytic properties of the modified electrodes

Cyclic Voltammetric (CV) technique provides a useful approach to the investigation of the electrochemical behaviors of the modified electrodes. Fig. 3 displays the CV responses of the electrodes in the mixture solution of 0.1 M KCl and 5 mM K₃Fe (CN)₆. The anodic and cathodic peak potential separations (ΔE_p) of the probe of (K₃Fe (CN)₆) at bare CPE (a), CILE (b), MWCNT/CILE (c), TiO₂/CILE (d), and MWCNT/TiO₂/CILE (e) are 536, 330, 232, 267, and 207 mV, respectively.

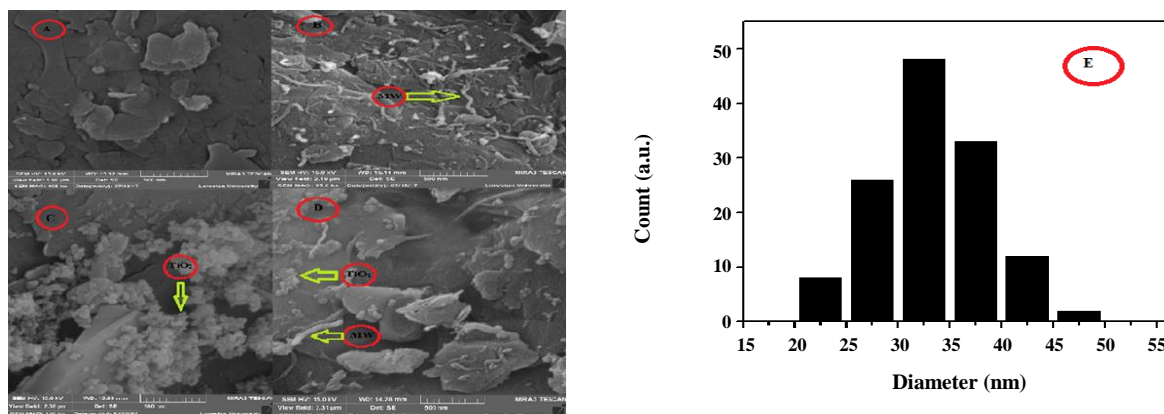


Fig. 1: SEM images of CILE (A), MWCNT/CILE (B), TiO₂/CILE (C) and MWCNT/ TiO₂/CILE (D) histogram of the particle size distribution of nanoparticles(E)

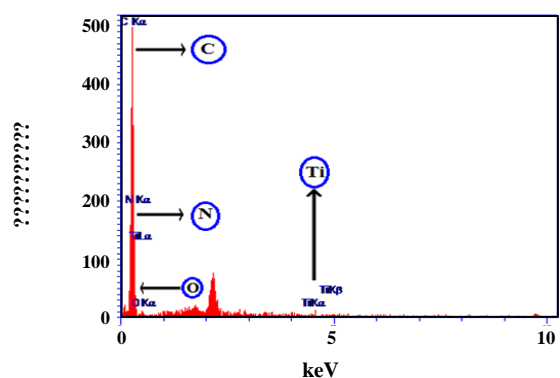


Fig. 2: EDX spectrum of MWCNT/ TiO₂/CILE nanocomposite.

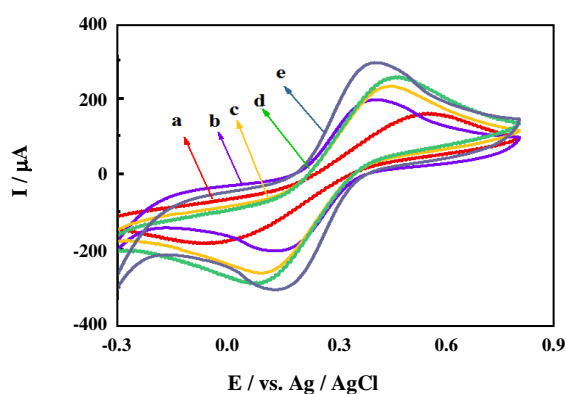


Fig. 3: CVs of bare CPE(a), CILE(b) MWCNT/ CILE (c), TiO₂/CILE (d) and MWCNT/TiO₂/CILE(e) in a 5mM K₃Fe(CN)₆ and 0.1M KCl mixture solution and scan rate: 25 mV/s.

The semiconducting nature of MWCNTs has caused the slowly increasing background current of the modified electrode, increasing effective surface area for electrode

and electrostatic interactions of MWCNT and CILE have provided more stable and excellent biocompatibility, therefore the peak potential of the MWCNT/ CILE (c) has shifted to less positive values in Fig 3[8]. The decreased potential separation of MWCNT/TiO₂/CILE indicated the enhanced rates of electron transfer and reduced overpotentials caused by the electrostatic interactions between MWCNTs and TiO₂ NPs [35-36]. Moreover, the “cation-π” interaction between the cationic part of IL (HPFP) and π in the MWCNTs and MWCNT/TiO₂/CILE nanocomposite provided excellent biocompatibility, a large aspect ratio, and high electrical conductivity, thus ensuring its wide applicability in electrochemical sensors [22,37-39]. On other hand, an increment in the current peak at MWCNT/TiO₂/CILE in comparison with MWCNT/ CILE (c) and TiO₂/CILE is due to its several advantages such as highly effective surface area, increased sensitivity, and enhanced mass transport.

The Randles–Sevcik equation

$$I_{pa} = (2.69 \times 10^5) n^{3/2} A D^{1/2} C^* v^{1/2}$$

was employed to detect the electroactive surface area of the modified electrode in the mixture solution of 0.1 M KCl and 5 mM K₃Fe(CN)₆.

where n shows the number of electron transfer, I_{pa} denotes the redox peak current, A indicates the electroactive surface area (cm²), D represents the diffusion coefficient of K₃Fe(CN)₆ in the 0.1 M KCl solution (D=0.76×10⁻⁶ cm²/s), C* demonstrates K₃ [Fe(CN)₆] concentration (mol/L), and v stands for the scan rate (V/s). The active surface areas of bare CPE, CILE, MWCNT/CILE, TiO₂/CILE, and MWCNT/TiO₂/CILE were 0.0365, 0.243, 0.275, 0.281, and 0.540 cm², respectively. The results could be ascribed to the synergistic effects of the non-material application.

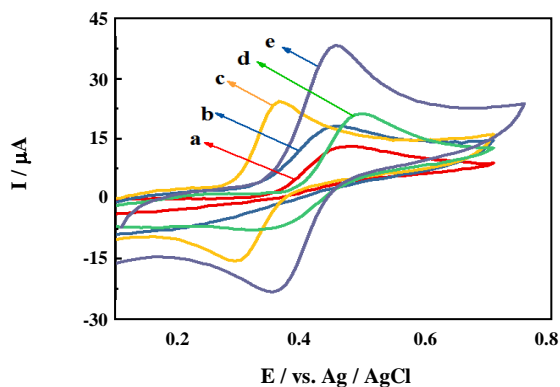


Fig. 4: Cyclic voltammograms of 100 μM of Ac in PBS (pH 6.0) with a scan rate of 25 mVs^{-1} at the surface of bare CPE(a), CILE (b), MWCNT/ CILE (c), TiO_2/CILE (d) and MWCNT/ TiO_2/CILE (e).

The CVs of bare CPE (a), CILE (b), MWCNT/CILE (c), TiO_2/CILE (d), and MWCNT/ TiO_2/CILE (e) in the presence of Ac at the pH value of 6.0 and scan rate of 25 mV/s are displayed in Fig. 4. CVs for Ac at bare CPE (a), CILE (b), MWCNT/CILE (c), TiO_2/CILE (d), and MWCNT/ TiO_2/CILE (e) were observed to have the current responses of 12.6, 18.3, 20.9, 19.1, and 38.9 μA , respectively.

The anodic peak current of Ac at MWCNT/ TiO_2/CILE compared to those of the other types of hybrid electrodes was observed to have further enhancement, which was caused by not only the electrostatic interactions between MWCNTs and TiO_2 NPs, but also the “cation- π ” interaction between the cationic part of IL (HPFP) and π in the MWCNTs. Also, the combination of the unique properties of MWCNT/ TiO_2 and CILE and their synergistic interactions led to a large enhancement of the sensing surface for enhanced determination of Ac.

The solution pH effect

The pH of the solution played a significant role in the CV responses of the modified electrode. CV helped us investigate the impacts of the pH range of 2.0-9.0 on the peak potential of Ac solution (50 μM) at the presence of MWCNT/ TiO_2/CILE nanocomposite (Fig. 5A). Proton's involvement in the proposed system was deduced from the elevated pH of the solution leading to the gradual enhancement of the redox peak currents associated with a shift of both the anodic and cathodic peak potentials. This is indicative of the involvement of Ac electrode reaction at

MWCNT/ TiO_2/CILE nanocomposite in the transfer process of protons.

Fig. 5B shows a gradual increase in the maximum current by augmenting the pH up to a value of 6 and its decline at higher pH values. Thus, the optimal pH of 6.0 was selected for Ac determination.

Also, the linear regression equations of $E_{pa} = -0.059 \text{ pH} + 0.8171$ $R^2=0.996$ and $E_{pc} = -0.072 \text{ pH} + 0.798$ with $R^2=0.995$ were achieved with the E_{pa} and E_{pc} slope approaching very close to the theoretical value of -0.059 V pH^{-1} (Fig. 5C).

Hence, these results were in agreement with the Nernst equation, indicating that the reaction Ac on the MWCNT/ TiO_2/CILE surface had equal numbers of electrons and protons.

Scan rate effect

CV further helped in the recognition of the dominant type of mass transport and the scan rate impact on 50 μM of Ac electro-oxidation at the MWCNT/ TiO_2/CILE surface over a range of 10-100 mV/s (Fig. 6A). As shown in the figure 6A, A good linear relationship was achieved between both the anodic and cathodic peak currents and the scan rate via the regression equations as follows: $I_{pa} (\mu\text{A}) = 0.70 v + 10.01$ ($R^2=0.999$), and $I_{pc} (\mu\text{A}) = -0.50 v - 5.57$ ($R^2=0.997$) indicating the adsorption-controlled process occurring on the electrode surface (Fig. 6B).

On the other hand, according to Laviron theory [40] for an adsorption-controlled and quasi-reversible interfacial reaction, the relationship between ΔE_p and $\text{Log} v$ is defined by the following equation:

$$\Delta E_p = K + [0.059 / (\alpha) n] \log v \quad (1)$$

Therefore, the regression equation of ΔE_p vs. $\text{Log} v$ was defined as follows (Fig. 6C):

$$\Delta E_p = 0.059 \log v - 0.0019 \quad \text{associated with } R^2=0.996 \quad (2)$$

Based on the mentioned equation and considering the transfer coefficient of $\alpha=0.5$ for the totally irreversible adsorption-controlled process, the number of electron transfer (n) in the electro-oxidation phase of Ac was calculated to be 2.

According to Bard and Faulkner [41], α can be determined via the following equation:

$$\Delta E_p = E_p - E_{p/2} = 48 / \alpha n \quad (3)$$

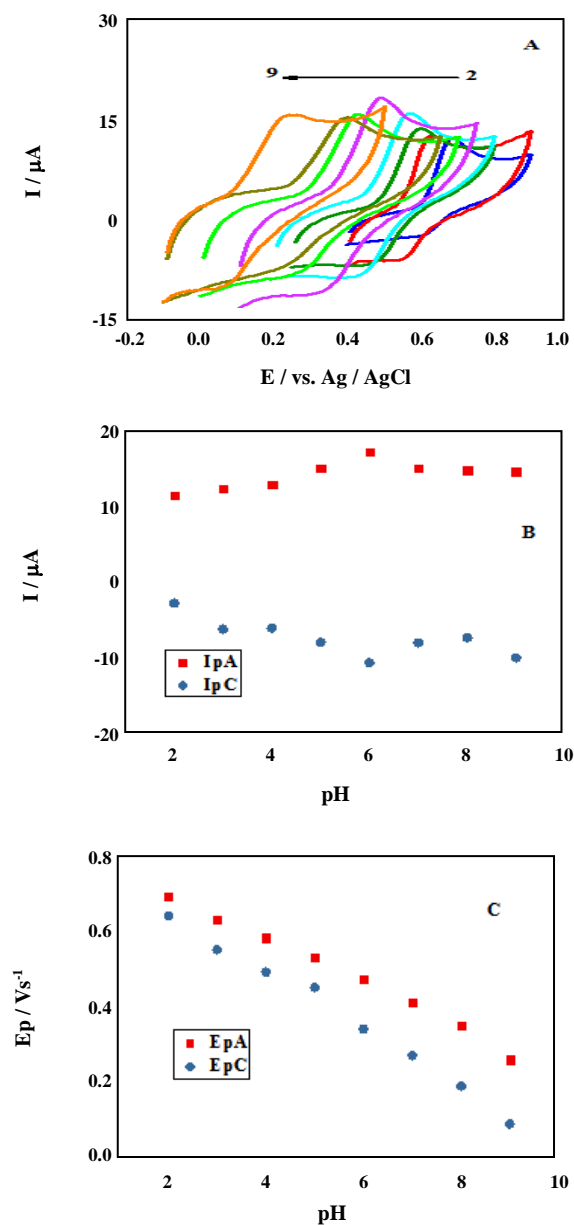


Fig. 5. (A) Cyclic voltammograms of MWCNT/TiO₂/CILE in containing 50 μM of Ac at various pH values (2.0–9.0), and scan rate 25 mV/s (B) Dependence of the anodic peak and cathodic peak currents as a function of solution pH. (C) The linear relationship between peak potentials and pH values

Where $E_{p/2}$ is the potential whose current is half of the peak value. The value of 50 mV was obtained for ΔE_p whose substitution in the above equation resulted in a value of 0.96 for αn . Accordingly, the value of α was achieved to be 0.5. Finally, n was found to

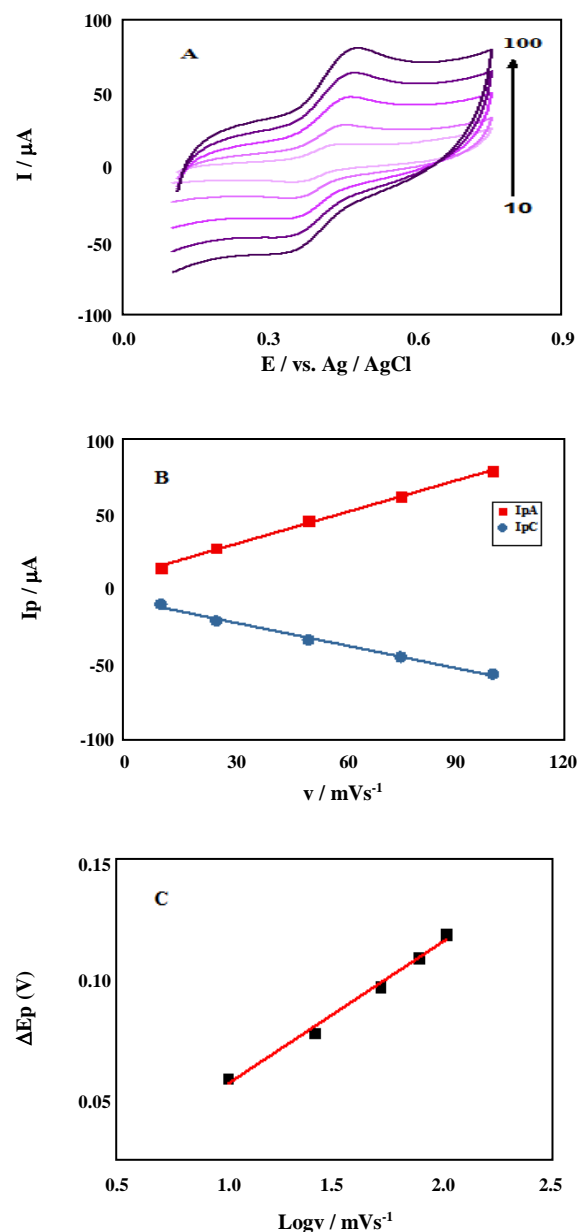
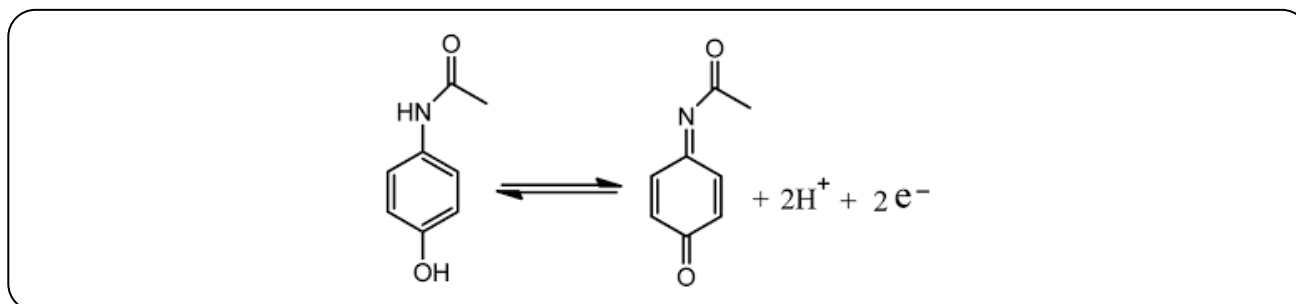


Fig. 6: (A) CVs for MWCNT/TiO₂/CILE in pH 6.0 containing 50 μM of Ac with scan rates as 10, 25, 50, 75, and 100 mV/s respectively. (B) The linear relationship of the anodic peak and cathodic peak currents vs. scan rate, (C) Tafel plot derived from the current potential curve recorded at scan rate 10 mV/s, (D) the plot of ΔE_p vs. $\log v$

have a value of 1.92 by putting the value of $\alpha=0.5$ in this equation, which is approximately 2. Based on these findings, a plausible mechanism was found for the reaction of Ac, the pathway of which is illustrated in Scheme 1.



Scheme 1: AC oxidation mechanism

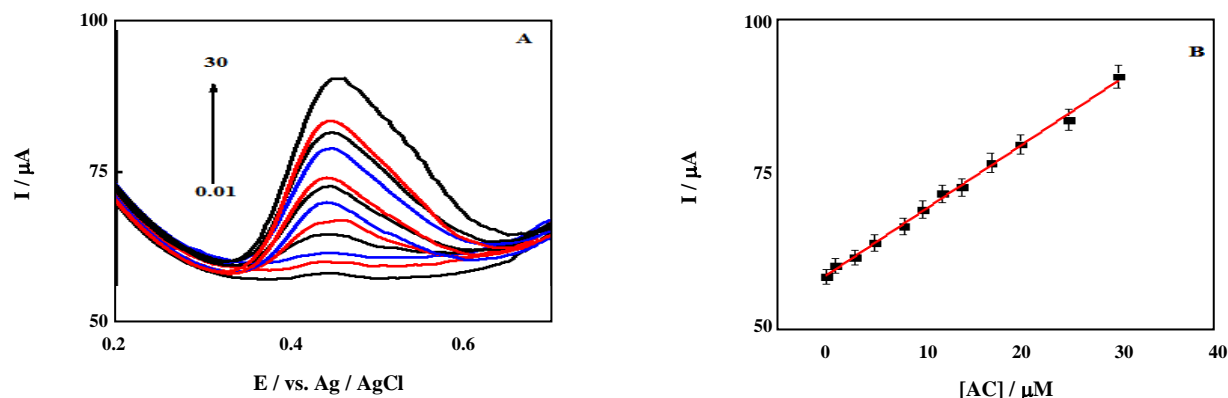


Fig. 7: (A) Square wave voltammograms with increasing concentrations of Ac in pH 6.0 at MWCNT/TiO₂/CILE: (a) 0.01, (b) 1; (c) 3; (d) 5; (e) 8; (f) 10; (g) 12; (h) 14; (i) 17.0; (j) 20.0; (k) 25 and (l) 30 μM. (B) Plot of the anodic peak current vs. concentrations of Ac.

Ac determination at MWCNT/TiO₂/CILE

Square Wave Voltammetry (SWV) has a current sensitivity of significantly higher than CV. Therefore, SWV was employed for Ac determination on the surface of MWCNT/TiO₂/CILE nanocomposite in the PBS at a pH value of 6 (Fig. 7A). The results demonstrated the direct proportionality of the peak current to Ac concentration within the range of 0.01–30 μM along with the Limit of Detection (LOD=3Sb/m) of 0.003 μM and Limit of Quantitation (LOQ=10Sb/m) of 0.01 μM. The linear regression equation illustrated $I_p (\mu\text{A}) = 1.05 [\text{Ac}] + 58.1$, ($R^2=0.997$) (Fig. 7B)

The method applied for Ac determination on MWCNT/TiO₂/CILE surface was compared with the other previously reported analytical methods, the results of which are displayed in Table 1. As can be seen, the proposed sensor exhibited a wide linear range with a LOD comparable to those of the other reported methods. This method depicted its appropriate applicability for Ac detection with a wider linear range and higher sensitivity

at lower concentrations compared to any other analytical approaches.

This result showed that Ac determination at MWCNT/TiO₂/CILE surface is practicable due to the high kinetic rate of electron exchange and good electrocatalytic activity of MWCNT/TiO₂/CILE nanocomposite.

The proposed method's stability, repeatability, and reproducibility

MWCNT/TiO₂/CILE stability was studied by keeping it at room temperature for 21 days. Then, the current response of Acetaminophen was achieved and compared with those obtained before storing. The results showed that the current response of the proposed electrode underwent only a slight change, thus indicating excellent stability. MWCNT/TiO₂/CILE repeatability was evaluated by repeating Ac measurement (5 μM). The used electrode was subjected to 6 successive CV sweeps of 0.2–0.7 V at 0.025 V/s in the PBS (pH 6) so as to eliminate

Table 1: A comparison between the proposed and other methods for Ac determination.

Method	Electrode	Linear range (μM)	Detection limit (μM)	Refrance
DPV	TiO ₂ NP-MCPE	0.07-100	0.018	[42]
SWV	CoFe ₂ O ₄ /Gr/CPE	0.03-12.0	0.025	[43]
DPV	MWCNT/ZnO-Au/GCE	0.05-20	0.009	[44]
DPV	ZONM/CPE	1.0-2500	0.91	[45]
SWV	NiFe ₂ O ₄ /Gr/CPE	0.01-9.0	0.0036	[46]
SWV	fMWCNT-CoPc/AuNPs/GCE	1.49-107.0	0.135	[47]
DPV	GA@O-CQDs	0.001-10	0.038	[48]
Amperometry	RGO-gold dendrite/GCE	0.07-3000	0.005	[49]
DPV	MWCNT- β -CD/GCE	0.05-1,1-300	0.0115	[50]
CV	ploy(DA)/GCE	0.02-500	0.0067	[51]
SWV	MWCNT/IL/TiO ₂ /CPE	0.01-30.0	0.003	This work

* DPV: Differential pulse voltammetry, SWV: Square wave voltammetry, TiO₂NP-MCPE: TiO₂ nanoparticles modified carbon paste electrode, ZONMCPE: ZrO₂ nanoparticle modified carbon paste electrodes, MWCNT- β -CD/GCE: multi-walled carbon nanotubes with β -cyclodextrin (β -CD), GA@O-CQDs: graphene aerogel@octadecylamine-functionalized carbon quantum dots, ploy (DA)/GCE: Diglycolic acid (DA) polymer

Table 2: Interferences of some foreign species on Ac determination (10.0 μM) under the optimized conditions

Foreign species	Tolerant limits ($W_{\text{substance}}/W_{\text{Ac}}$)
Ascorbic acid, Cysteine, Dopamine, L-Dopa	200
Uric acid	100
Fructose, Urea, Oxalic acid, Citric acid, L-histidine, glucose, sucrose	500

any adsorbents after each determination. The measurements revealed good repeatability associated with an RSD of 1.94%. Also, the reproducibility of the MWCNT/TiO₂/CILE sensor was assessed using 6 independently prepared sensors in the same fabrication process. The RSD value obtained for Ac determination was 2.52%. The results were indicative of the good reproducibility of MWCNT/TiO₂/CILE nanocomposite for Acetaminophen determination.

Interference studies

The impacts of the different foreign materials on Ac determination (10 μM) were evaluated under optimum conditions. In addition, some biologically coexistent agents in the body fluids were assessed. The maximal concentrations of the interfering substances provided the tolerance limit causing a relative error of nearly 5% for Acetaminophen determination. therefore, we investigated the selectivity of the MWCNT/TiO₂/CILE sensor electrode in co-existed materials which were ascorbic acid

(200-fold), cysteine (200-fold), dopamine (200-fold), L-dopa(200-fold), uric acid (100-fold), fructose (500-fold), urea(500-fold), Oxalic acid(500-fold), Citric acid (500-fold), L-histidine(500-fold),glucose (500-fold), sucrose (500-fold), and L-serine(600-fold) on the determination of AP (10 μM). These results (in Table 2) confirmed that the simultaneous presence of substances has no impact on the selective detection of Ac.

Ac analysis in real samples

To evaluate the ability of MWCNT/TiO₂/CILE sensor in real samples, it was examined on commercial tablets and human plasma samples. Ac concentrations were measured in the real samples by using the standard addition method according to the above equation of roagation rate obtained and thus measuring the SWV responses. The analysis results of the studied samples are exhibited in Table 3. The fabricated electrode was assessed in terms of its practical usefulness through Ac analysis in various tablet and human plasma samples.

Table 3. Ac determination in the real samples under optimum conditions (n=6)

Sample	Added (μM)	Found (μM)	Recovery (%)
Tablet(325 mg)	5	4.9 \pm 0.3	98
Plasma	5	5.2 \pm 0.2	104
Plasma	5	4.7 \pm 0.4	94

CONCLUSION

A simple electrochemical procedure was applied in the current research for analytically determining Ac on MWCNT/TiO₂/CILE surface. The comparisons of Acetaminophen electrochemical behaviors at bare CPE, CILE, MWCNT/CILE, TiO₂/CILE, and MWCNT/TiO₂/CILE were suggestive of the significant enhancements of its current signals induced by MWCNT/TiO₂/CILE. Therefore, the combination of the unique properties of MWCNT and TiO₂ and their interaction with the IL and their synergistic interactions led to a large enhancement of the Ac voltammetric signal. Ac displayed linear SWV responses within the dynamic range of 0.01-30.0 μM and LOD of 0.003 μM . The modified electrode exhibited good repeatability and reproducibility for the determination of Ac concentrations. Furthermore, the mentioned electrode was successfully utilized to detect Ac in the plasma and tablet samples. Finally, no considerable interferences with Ac determination were observed via the electrochemical sensor as indicated by the results of the interference studies.

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