ELECTROCHEMICAL DETERMINATION OF ACETAMINOPHEN AT THE SURFACE OF A GLASSY CARBON ELECTRODE MODIFIED WITH MULTI-WALLED CARBON NANOTUBE

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ABSTRACT

A multi-walled carbon nanotubes (MWCNTs) film coated glassy carbon electrode (GCE) was fabricated, and the electrochemical behavior of acetaminophen (AAP) was studied in Britton–Robinson (BR) buffer (pH 7.0), using cyclic voltammetry (CV), square-wave voltammetry (SWV) and differential pulse voltammetry (DPV). Cyclic voltammograms of AAP showed enhanced redox responses for the MWCNT/GCE with respect to the bare GCE. The anodic peak potential shifted to less positive values by increasing the pH. The electrochemical oxidation of AAP at MWCNT/GCE was quasi-reversible and diffusion-controlled. Experimental parameters, such as pH, scan rate, SW frequency and step height, were optimized for AAP measurement. Under the optimum pH of 7.0 in 0.1 M BR buffer solution, the DPV anodic peak current showed a linear relation versus AAP concentration in the range of 7.9×10^-7 to 3.4×10^-4 M with a detection limit of 3.3×10^-5 M with a detection limit of 2.1×10^-6 M for SWV with a detection limit of 2.1×10^-5 M. This method possesses many advantages such as low detection limit, fast response, low cost and simplicity.

Keywords: Acetaminophen; Carbon nanotubes; Glassy carbon electrode; Electrochemical determination

INTRODUCTION

Carbon nanotubes (CNTs) are a novel nanoscale material, mainly consisting of single-wall carbon nanotubes (SWCNTs) and multi-walled carbon nanotubes (MWCNTs)1-2. CNTs have attracted considerable attention due to their extraordinary structural, mechanical, electrical, and electrochemical properties as well as their promise in the field of materials science3. Due to their unique structure, CNTs can behave electrically as a metal or as a semiconductor. The subtle electronic behavior of CNTs demonstrates that they have the ability to promote electron-transfer reactions when used as electrode materials4. Several types of CNT electrodes have been reported, including CNT paste electrodes5, CNT film-coated electrodes6,7, CNT powder microelectrodes8 and CNT paper electrodes9.

Acetaminophen (N-acetyl-p-aminophenol or paracetamol) (AAP) is a common analgesic and antipyretic drug that is used for the relief of fever and headaches, as well as other minor aches and pains. It is an attractive alternative drug for children and adults that are sensitive to aspirin10. At the recommended dosage, there are no side effects. However, overdoses due to liver and kidney damage can be harmful. Therefore, it is very important to establish a simple, fast, sensitive and accurate detection method for the determination of AAP. Many methods have been described for AAP determination, such as titrimetry11, spectrophotometry12, liquid chromatography13 and UV–Vis spectrophotometry14,15. Electrochemical methods, owing to their low cost and reduced time consumption, are also popular for this application. Among electrochemical methods, AAP has been assessed by voltammetry using several techniques, including C6-modified glassy carbon electrodes (GCEs)16, GCEs coated with a SWCNT-dicetyl phosphate film17, PANI-MWCNT modified electrodes18 and carbon-coated nickel-modified electrodes19. Electrode surface modification and pretreatments have been widely used to improve the electrochemical responses of biological compounds20. For example, CNT-modified GCEs provide a stable and sensitive electrochemical response for phenols21, NADH22, estrogenic phenolic compounds23,24, dopamine25, uric acid26 and tetracycline27.

In the current study, a MWCNTs modified GE was fabricated and used to determine AAP. The electrochemical behavior of AAP suggested that MWCNTs modified GE exhibits an obvious electrocatalytic effect on the oxidation of AAP, since it greatly enhances the oxidation peak current of AAP as well as lowering its oxidation overpotential. After optimizing the experimental parameters, this electrode has used for the direct measurement of AAP in tablets and syrups. This method possesses many advantages such as a low detection limit, fast response, low cost and simplicity.

MATERIAL AND METHODS

Reagents and chemicals

AAP was purchased from the Farabi Pharmaceutical Company. The Britton Robinson (BR) buffer solution was comprised of phosphoric acid, boric acid and glacial acetic acid and its pH was adjusted with NaOH. MWCNTs with purity >95% (40-60 nm in diameter) were obtained from the Chinese Academy of Sciences. Generally, pristine MWCNTs contained 3% amorphous carbon, SWCNTs and graphite, requiring some purification pre-treatment before electro-analytical characterization. A 1.0×10^-3 M AAP standard solution was simply prepared by dissolving AAP in distilled water. Working solutions were prepared with this standard solution and using suitable dilutions with a 0.1 M BR buffer solution. BR buffer solution was also used as the supporting electrolyte.

Apparatus

Electrochemical measurements were carried out on a M273A Electrochemical Workstation (America, EG&G Corporation). A conventional three-electrode system was employed, consisting of a MWCNTs modified GE as a working electrode (Metrohm), a saturated calomel reference electrode (SCE) (Metrohm) and a Pt wire counter electrode (Metrohm). Solution pH values were determined using a 691 pH meter (Metrohm Swiss made) combined with glass electrode (Metrohm). Deionized water was formed with an ultrapure water system (smart 2 pure, TKA, Germany). MWCNTs was dispersed with an ultrasonic bath (SONOREX DIGITAL, 10P, BANDELIN). Data were collected at room temperature.

Fabrication of the modified electrode

Using ultrasonic agitation, 0.5 mg of purified MWCNTs was dispersed into 5 ml of distilled water for 30 min. Prior to modification, the GCE was polished with 0.05 mm alumina slurry and then cleaned ultrasonically in double-distilled water. Subsequently, the GCE was coated with 20 µL of MWCNT suspension and the solvent was evaporated in air.

RESULTS AND DISCUSSION

Voltammetric behavior of AAP on the MWCNT/GCE

The electrochemical behavior of AAP at unmodified GCE and MWCNT film coated GCE was examined by CV. Figure 1 shows the cyclic voltammograms of 5.0×10^-3 M AAP on a modified (a) and unmodified GCE (b) in the potential range of 0.0 to 0.7 V in 0.1 M BR buffer (pH 7.0). Figure 1c shows the cyclic voltammogram of the modified electrode in the absence of AAP. As can be seen, at the unmodified GCE (Figure 1b), AAP shows irreversible behavior with a relatively weak oxidative peak at Ep = 0.447 V, and no reduction peak in reverse scan.

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The electrochemical behavior of AAP was investigated over the pH range from 4 to 10 in 0.1 M BR buffer solution. Figure 3 shows cyclic voltammograms of \(5.0 \times 10^{-5}\) M AAP in 0.1 M BR buffer at different pHs (from 4 to 10). Inset, plot of \(E_p\) versus pH. Scan rate = 100 mV s\(^{-1}\).

**Effect of DPV and SWV parameters**

The peak current obtained in DPV and SWV is dependent on several instrumental parameters, including pulse height, frequency, scan increment and scan rate. These parameters are interrelated and have a combined effect on the response. In this work, these parameters were found to have little effect on the peak potential. For SWV, when the pulse height was varied in the range between 10 and 300 mV, the peak currents increased with increasing pulse height. However, the peak width was also increasing at the same time. This was particularly apparent when the pulse height was greater than 100 mV. Hence, 100 mV was chosen as the square-wave pulse height. The scan increment together with the frequency defines the effective scan rate. Hence, an increase in either the frequency or the scan increment results in an increase in the effective scan rate. The response for AAP increased with a SW frequency up to 30 Hz, above which the peak current was obscured by a large residual current. By fixing the frequency at 30 Hz, the effect of scan increment was studied. At scan increments greater than 3 mV, the resolution and sensitivity decreased. However, at a scan increment of 3 mV, a response was recorded. Overall, the optimized parameters are summarized in Table 1.

Table 1. Optimum experimental condition for SWV and DPV.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Range studied</th>
<th>Optimum value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SWV</td>
<td>DPV</td>
</tr>
<tr>
<td>Pulse height (mV)</td>
<td>10-300</td>
<td>50-300</td>
</tr>
<tr>
<td>Frequency (Hz)</td>
<td>10-100</td>
<td>---</td>
</tr>
<tr>
<td>Scan increment (mV)</td>
<td>2-10</td>
<td>2-10</td>
</tr>
<tr>
<td>Scan rate (mVs(^{-1}))</td>
<td>---</td>
<td>50-200</td>
</tr>
</tbody>
</table>

**Calibration curve**

The relationship between the oxidation peak current and AAP concentration was examined using DPV and SWV and two linear dynamic ranges were observed. In DPV method, the first linear dynamic range was between \(7.9 \times 10^{-7} - 5.7 \times 10^{-5}\) M and the second was between \(5.7 \times 10^{-5} - 3.4 \times 10^{-4}\) M (Figure 4). The relationship between peak current and concentration can be described with the following linear regression equations for the aforementioned concentration ranges for the first and second linear dynamic ranges:

\[
\text{ip}_{\text{p}} (\mu A) = 0.165c (\mu M) + 0.0126 \\
\text{(r = 0.9996)}
\]

\[
\text{ip}_{\text{p}} (\mu A) = 0.0447c (\mu M) + 12.365 \\
(\text{r = 0.9989})
\]
The first linear dynamic range was chosen for the determination of AAP with a detection limit of $3.3 \times 10^{-7}$ M.

Figure 4: DPV of AAP on MWCNT/GCE in 0.1 M BR buffer (pH 7.0) at different AAP concentrations from $7.9 \times 10^{-7}$ to $3.4 \times 10^{-4}$ M: Inset, Linear relationship between $i_p$, and the concentration of AAP ($7.9 \times 10^{-7}$ to $5.7 \times 10^{-5}$ M).

Figure 5 shows SW voltammograms of AAP at various concentrations. The oxidation peak current of AAP was found to be proportional to AAP concentration over the ranges of $6.5 \times 10^{-7}$ to $5.8 \times 10^{-5}$ M and $5.8 \times 10^{-5}$ to $3.5 \times 10^{-4}$ M. The linear regression equations for the first and second linear dynamic ranges are expressed as:

$$i_p (\mu A) = 0.0581c (\mu M) + 0.3236 \quad (r = 0.9998)$$
$$i_p (\mu A) = 0.0298c (\mu M) + 2.906 \quad (r = 0.9987)$$

When the signal-to-noise ratio was 3, the detection limit was $2.1 \times 10^{-7}$ M, which is lower than the DPV value of $3.3 \times 10^{-7}$ M. Which values of detection limit is comparable to values reported by other research groups for oxidation of APP at the surface of modified electrodes (Table 2). SWV calibration curves of AAP for the first and second linear dynamic ranges are showed in Figures 6A and 6B, respectively.

Table 2. Comparison of the efficiency of some modified electrodes used in the electro-oxidation of APP.

<table>
<thead>
<tr>
<th>Electrode</th>
<th>Method</th>
<th>pH</th>
<th>Detection limit (M)</th>
<th>Dynamic range (M)</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MWCNT/paste electrode</td>
<td>SWV</td>
<td>7.0</td>
<td>$1.1 \times 10^{-6}$</td>
<td>$1.0 \times 10^{-5}$ to $1.0 \times 10^{-4}$</td>
<td>31</td>
</tr>
<tr>
<td>5-amino-3',4'-dimethyl-biphenyl-2-ol-CNT/paste electrode</td>
<td>SWV</td>
<td>7.0</td>
<td>$2.0 \times 10^{-7}$</td>
<td>$4.0 \times 10^{-7}$ to $9.0 \times 10^{-6}$</td>
<td>32</td>
</tr>
<tr>
<td>Nano Pt-MWCNT/paste electrode</td>
<td>DPV</td>
<td>7.0</td>
<td>$1.7 \times 10^{-7}$</td>
<td>$5.0 \times 10^{-6}$ to $1.0 \times 10^{-4}$</td>
<td>33</td>
</tr>
<tr>
<td>Poly(acid yellow 9)-TiO$_2$/GCE</td>
<td>DPV</td>
<td>7.0</td>
<td>$2.0 \times 10^{-6}$</td>
<td>$1.2 \times 10^{-5}$ to $1.2 \times 10^{-4}$</td>
<td>34</td>
</tr>
<tr>
<td>poly (calconcarboxylic acid)/GCE</td>
<td>DPV</td>
<td>6.0</td>
<td>$1.0 \times 10^{-8}$</td>
<td>$1.0 \times 10^{-7}$ to $1.0 \times 10^{-6}$</td>
<td>35</td>
</tr>
<tr>
<td>MWCNT/ GCE</td>
<td>DPV</td>
<td>7.0</td>
<td>$3.3 \times 10^{-7}$</td>
<td>$7.9 \times 10^{-7}$ to $3.4 \times 10^{-6}$</td>
<td>This work</td>
</tr>
</tbody>
</table>

Figure 6: SWV calibration curves of AAP covering different concentration ranges with a MWCNT/GCE. A, $6.5 \times 10^{-7}$ to $5.8 \times 10^{-5}$ M; B, $5.8 \times 10^{-5}$ to $3.5 \times 10^{-4}$ M.

Stability and reproducibility of the MWCNT/GCE

The reproducibility of MWCNT-film modified GCEs was examined by repeating the measurement of $1.0 \times 10^{-5}$ M AAP. After each determination, the used modified electrode underwent five successive cyclic voltammetric sweeps between 0.20 and 1.00 V at a scan rate of 50 mV/sec$^{-1}$ in 0.1 M BR (pH 7.0), to remove any adsorbents and yield a reproducible electrode surface. The relative standard deviation (RSD) of ten measurements was 1.3%. The long-term stability of the MWCNT film-coated GCE was also tested by measuring the reduction peak current at a fixed AAP concentration of $1.0 \times 10^{-5}$ M over a period of 3 weeks. After 3 weeks, the current response only decreased by 3.2%. These results indicate that the electrode has excellent reproducibility and long-term stability, making it attractive for the fabrication of chemical sensors.
Interference
The effect of possible interference was investigated by the addition of other compounds to a solution containing 1.0×10^{-6} M AAP in 0.1 M BR electrolyte. Each possible contaminant was first added to yield a concentration identical to that of AAP. Subsequently, another addition was made so that the interfering concentration was 10 times that of AAP. Ascorbic acid, uric acid, penicillin, aspirin and amoxicillin were tested as interferents. Uric acid, penicillin, aspirin and ascorbic acid were found to cause less than a 5% increase in the AAP current peak height, even when present in 10-fold excess. The presence of amoxicillin in 10-fold excess of AAP was sufficient to cause a 10% decrease in AAP signal.

Sample analysis
The MWCNT-modified GCE was used to determine AAP in tablets. AAP content was calculated by the standard addition method and the results are shown in Table 3. Results obtained by SWV are in good agreement with DPV results, as well as with the declared AAP content. The recovered ratio indicates that the determination of AAP using MWCNT/GCEs is effective and sensitive.

Table 3. Determination of AAP in tablets.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Declared (µM)</th>
<th>Detected (µM)</th>
<th>Recovery (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen</td>
<td>7.00</td>
<td>7.06</td>
<td>100.9</td>
</tr>
<tr>
<td>(325 mg)</td>
<td></td>
<td>6.40</td>
<td>91.4</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>7.00</td>
<td>7.20</td>
<td>102.8</td>
</tr>
<tr>
<td>Codeine (300 mg)</td>
<td></td>
<td>6.60</td>
<td>94.3</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>10.00</td>
<td>9.50</td>
<td>95.0</td>
</tr>
<tr>
<td>(500 mg)</td>
<td></td>
<td>9.30</td>
<td>93.0</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>80.00</td>
<td>86.00</td>
<td>107.5</td>
</tr>
<tr>
<td>Syrup</td>
<td></td>
<td>87.00</td>
<td>108.7</td>
</tr>
</tbody>
</table>

CONCLUSION
Utilizing the unique properties of MWCNTs, such as their high specific surface area and subtle electronic properties, MWCNT-modified glassy carbon electrodes in DPV and SWV techniques were used for the determination of AAP. The detection limit for SWV was 2.1×10^{-6} M, which is lower than the DPV detection limit of 3.3×10^{-5} M, based on this work, a simple, rapid and sensitive method (i.e., SWV) was developed for AAP determination.

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REFERENCES