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CYCLIC VOLTAMMETRIC DETERMINATION OF ACETAMINOPHEN IN PARACETAMOL TABLETS

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ABSTRACT

A method using cyclic voltammetry has been developed for the determination of acetaminophen in paracetamol tablets. The peak current from acetaminophen in 0.10 mol L^{-1} phosphate buffer pH 7.0 was measured with a glassy carbon electrode versus Ag/AgCl. The optimum step potential and scan rate were found to be 0.0005 V and 0.1000 V/s, respectively. The linear calibration range was 3-240 μg ml^{-1}, and the detection limit and recovery were 3.0 μg ml^{-1} and 99.1%, respectively. The results have been compared with those obtained by the USP XXII official method.

KEYWORDS: Acetaminophen; paracetamol; cyclic voltammetry; glassy carbon electrode

1. INTRODUCTION

Paracetamol (acetaminophen) is widely used as an analgesic and as an antipyretic drug. Many assays have been described for acetaminophen including titrimetry [1], chromatography [2-4], fluorometry [5], colorimetry [6-9], UV spectrophotometry [10], and various modes of electrochemistry [11-19]. Although the electrochemical oxidation of paracetamol at a glassy carbon electrode has been in the literature for some time [15] only a few applications of its use in differential pulse voltammetry have been reported; for determination of the drug in blood plasma and in a single type of tablet [16] and in a variety of drug formulations containing paracetamol [14]. Recently the differential pulse voltammetric behaviour of some drugs including paracetamol at various conducting polymers [12] and at pumice mixed carbon electrodes [17] have been examined and reviewed [18].

Herein we report a novel, simple, precise and sensitive cyclic voltammetric method utilizing a glassy carbon electrode vs. Ag/AgCl for the assay of acetaminophen was reported. The method was applied successfully to assay of acetaminophen in paracetamol tablets. The work was carried out to provide a low capital cost, inexpensive to operate alternative to a UV spectrophotometric assay and also to avoid the use of organic solvent.

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2. MATERIAL AND METHOD

2.1 Apparatus

Voltammograms were recorded with Potentiostat PGSTAT 20 (Autolab), interfaced to 663 VA stand (Metrohm) and Socos computer. A three-electrode configuration was used with a glassy carbon electrode (Metrohm) as the working electrode, a silver-silver chloride reference electrode (Metrohm) and a platinum wire as the auxiliary electrode (Metrohm). The working electrode was pretreated by polishing it with an alumina-water slurry, followed by washing in an ultrasonic bath.

2.2 Reagents and solutions

All reagents were of analytical reagent grade and ultra pure water (prepared using a Millipore. Model ZF0058008 coupled with a Millpore ZF050UV ultra pure water system) was used throughout. Acetaminophen standard solution 1000 μg ml^{-1} was prepared freshly, by dissolving 0.10 g of acetaminophen (Fluka, ≥98% by HPLC) in 100.00 ml of warm water. More dilute solutions were prepared by dilution with 0.10 mol L^{-1} phosphate buffer solution pH 7.0, as required. The solutions were stored in a cool, light protected cool location. Phosphate buffer solution pH 7.0 was prepared by adding 41.30 ml of 0.10 mol L^{-1} potassium dihydrogen phosphate into 58.70 ml of 0.10 mol L^{-1} disodium hydrogen phosphate.

2.3 General Procedure

A 20.00 ml of 30 μg ml^{-1} acetaminophen standard solution in 0.10 mol L^{-1} phosphate buffer pH 7.0 was pipetted into the voltammetric cell. The solutions were stirred with solvent-saturated nitrogen for 180 sesonds. The cyclic voltammograms were obtained by scanning the potentials from -0.3 to +1.5 V vs. Ag/AgCl at step potential of 0.0005 V and scan rate of 0.10 V/s. A typical cyclic voltammogram is shown in (Figure 1). A direct calibration curve and the standard addition method were both used to evaluate the content of acetaminophen in commercial samples of paracetamol tablets by cyclic voltammetry.

For the standard addition method, 20.00 ml of unknown sample solution in 0.1 mol L^{-1} phosphate buffer pH 7.0 was pipetted into the voltammetric cell. Five voltammograms were recorded after adding of 0.00, 0.50, 1.00, 1.50 and 2.00 ml of 1,000 μg ml^{-1} acetaminophen standard solution under the same conditions as above.

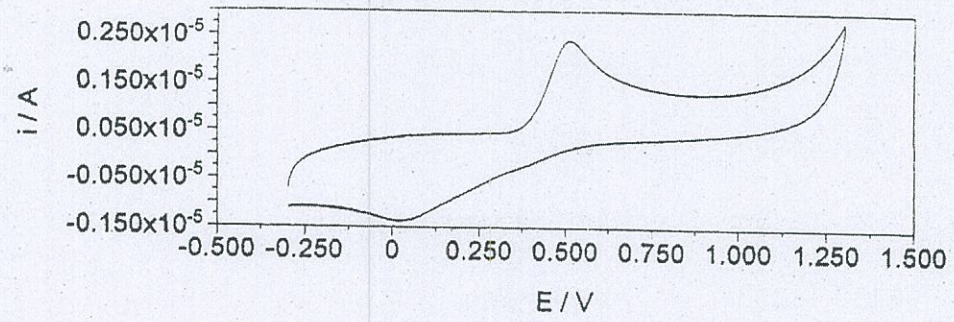

Figure 1 Cyclic voltammogram for 30 μg ml^{-1} acetaminophen in 0.10 mol L^{-1} phosphate buffer pH 7.0at a glassy carbon electrode vs. Ag/AgCl.

2.4 Procedure for paracetamol tablet samples

Twenty tablets of paracetamol were weighed and then powdered. A 0.10 g of powdered tablets was weighed accurately and placed into a 250 ml conical flask. A 75 ml of warm water was added into the flask. The sample was swirled to dissolve for 30 minutes and left cool. The sample solution was filtered through a filter paper (Whatman No.42) into 100 ml volumetric flask. The filtrate was make up to the volume. A 8 ml and a 3 ml aliquot of sample solutions was pipetted into 100 ml volumetric flasks and made up to volume with 0.10 mol L^{-1} phosphate buffer pH 7.0 for the direct calibration method and standard addition method, respectively. All the commercial samples of paracetamol tablets were produced in Thailand.

3. RESULTS AND DISCUSSION

3.1 Effect of parameters

The peak currents were examined as a function of the step potential and a scan rate. A step potential of 0.0005 V and a scan rate of 0.10 V/s were selected for the rest of the experiments because at these values the cyclic voltammograms were smooth and gave maximum peak currents. The anodic current was independent of the nitrogen gas purge time in the range of 0 to 420 seconds. Dissolved oxygen in solution did not affect the anodic peak current at potentials in the range of -0.30 V to 1.50 V. A nitrogen gas purge time of 180 seconds was used in subsequent work for the purpose of stirring.

3.2 The number of electrons involved in the oxidation of acetaminophen

The anodic peak potential, Ep,a from cyclic voltammograms of acetaminophen was measured at various pH of the media. A linear relationship was found between Ep,a and pH over the range 3-11. It was found that Ep,a (V vs Ag/AgCl) = -0.0315pH + 0.8175 ($r = 0.99$) with a slope of -0.0315 mV/pH unit. For an exact Nernstian response, the slope would be expected to be 0.0295 for two-electron and two-proton process. It was concluded, confirming earlier coulometric work [16], that acetoaminophen was electrochemically oxidised in a pH-dependent, two-electron, two-proton process to N-acetyl-p-quinoneimine. The maximum of anodic current was obtained at pH 7.0, using 0.01 mol L^{-1} phosphate buffer.

3.3 Calibration curve, precision, recovery and detection limit

The relationship between concentration and peak height anodic current was linear from 3 to 240 μg ml^{-1} of acetaminophen. A concentration range of 27 to 135 μg ml^{-1} of acetaminophen was chosen for calibration curve preparation because in this range the correlation coefficient was almost unity ($r = 0.9990$). For the electrode in use the peak current, $i(\mu A) = 1.1788 \times 10^{-7} c$ (μg ml^{-1}) - 1.665×10^{-6}. For the determination of 30 μg ml^{-1} of acetaminophen, the coefficient of variation was 0.80% based on 15 results and the recovery from the standard addition was 99.10% based on 5 results. The detection limit was 3.0 μg ml^{-1}.

3.4 Sample analysis

The content of acetaminophen in four commercial brands of paracetamol tablets were determined from five replicates of each sample. The results obtained are summarized in Table 1. The method was checked against results obtained by the USP XXII official spectrophotometric method and showed close agreement between the cyclic voltammetric method and the reference method. In addition, the results agreed well with the manufacturers stated values. The close agreement found between the cyclic voltammetric method and the reference method confirmed the absence of any from the small amounts of excipients present.

4. CONCLUSION

A cyclic voltammetric method was developed for the assay of acetaminophen involving oxidation at a glassy carbon electrode. This method was simple, requiring no separation stage, rapid and sufficiently precise for the routine assay of acetaminophen in paracetamol tablets.

Table 1 Assay of acetaminophen in paracetamol tablet samples

Sample	Declared acetaminophen content per tablet (mg)	Acetaminophen found by calibration curve, cyclic voltammetry* (mg)	USP XXII official method by calibration curve* (mg)	Acetaminophen found by standard addition, cyclic voltammetry* (mg)	USP XXII official method by standard addition* (mg)
"Daga" Hoescht "Paracetamol"	500.0	495.6±4.1	499.2±2.4	497.0±1.1	499.2±1.8
Thai Gov. Pharma. "Sara"	500.0	495.3±3.5	499.6±2.7	498.0±1.0	499.4±2.1
Nakorn Patana "Tylenol"	500.0	493.9±3.9	499.2±2.2	496.3±2.2	499.5±2.5
OLIC(Thai)	500.0	497.0±2.6	499.1±2.9	497.9±1.3	499.5±1.6

*mean ± 95% confidence acetaminophen for five replicates

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