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Assay of Acetaminophen in Paracetamol Tablets by Differential Pulse Voltammetry

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ABSTRACT

A simple and precise procedure using differential pulse voltammetry was developed for the assay of acetaminophen in paracetamol tablets. The peak current from acetaminophen in 0.1 mol L^{-1} phosphate buffer pH 7.0 was measured using a glassy carbon electrode and a Ag/AgCl reference electrode. The optimum step potential and modulation amplitude were 0.0020 and 0.0500 V, respectively. The linear calibration range was 0-300 $\mu g\ ml^{-1}$, the detection limit and recovery were 0.15 $\mu g\ ml^{-1}$ and 99.4%, respectively. The results were compared with those obtained by the U.S.P XXII official method.

Key words: acetaminophen; paracetamol, differential pulse voltammetry, glassy carbon electrode

INTRODUCTION

Paracetamol (acetaminophen) is widely used as an analgesic and antipyretic drug. Many assays have been described for acetaminophen including titrimetry (Blake and Shumaker, 1973), chromatography (McSharry and Savage, 1980; Carroll *et al.*, 1981 and Wang and Dewald, 1984), fluorometry (Oztunc, 1982), colorimetry (Murfin and Wragg, 1972; Belal *et al.*, 1979; Elsayed *et al.*,1979; Sane and Kamat, 1980; Afshari and Liu, 2001), UV spectrophotometry (Das *et al.*, 1989), and various modes of electrochemistry (Miner *et al.*, 1981; Navarro *et al.*, 1988; Bramwell *et al.*, 1990; Bramwell *et al.*, 1994; Gilmartin and Hart, 1994; Erdogdu and Karagozler, 1997; Lau *et al.*, 1989; Zen and Ting, 1997; Wang *et al.*, 2001 and Ozkan *et al.*, 2003). Although the electrochemical oxidation of paracetamol at a glassy carbon electrode has been in the literature for some times, (Miner *et al.*, 1981) 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 (Navarro *et al.*, 1988) and in a variety of drug formulations containing paracetamol (Lau *et al.*, 1989). Recently, the differential pulse voltammetric behaviour of some drugs including paracetamol at various conducting polymers (Erdogdu and Karagozler, 1997) and at pumice mixed carbon electrodes (Ozkan *et al.*, 2003) have been examined and reviewed (Wang *et al.*, 2001).

A simple differential pulse 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

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acetaminophen in paracetamol tablets. The procedure did not show bias, unlike the earlier method which showed 2.8-7.4 % positive bias, for simple paracetamol tablets (Lau *et al.*, 1989).

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.

MATERIALS AND METHODS

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 auxiliary electrode (Metrohm). The working electrode was pretreated by polishing it with an alumina water slurry, followed by washing in an ultrasonic bath.

Reagents and solutions

All reagents used were of analytical reagent grade and ultra pure water (Millipore Model ZFR0058008 coupled with a Millipore Model 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 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 mixing 41.30 ml of 0.10 mol L^{-1} potassium dihydrogen phosphate with 58.70 ml of 0.10 mol L^{-1} disodium hydrogen phosphate.

General procedure

A 20 ml aliquot of 30 μg ml^{-1} acetaminophen standard solution in 0.1 mol L^{-1} phosphate buffer pH 7.0 was pipetted into the voltammetric cell. The solution was stirred using solvent-saturated nitrogen for 180 seconds. Differential pulse voltammograms were recorded, scanning the potentials from -1.0 to +1.2 V vs. Ag/AgCl at a step potential of 0.002 V and modulation amplitude of 0.05 V. Acetaminophen is oxidized giving a peak current near +0.38 V (Fig.1). A direct calibration curve method and the standard addition method were used to evaluate the acetaminophen contents of commercial samples of paracetamol tablets.

For the standard addition method, 20 ml of an unknown sample solution in 0.1 mol L^{-1} phosphate buffer pH 7.0 was pipetted into the

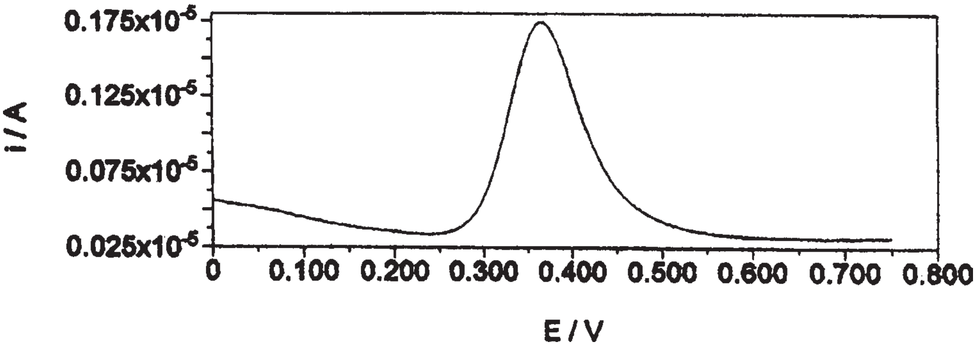

Figure 1 Differential pulse voltammogram for 30 μg ml^{-1} acetaminophen in 0.1 mol L^{-1} phosphate buffer pH 7.0 at a glassy carbon electrode vs. Ag/AgCl.

voltammetric cell. Five voltammograms were recorded using the conditions described above, after adding 0.00, 0.50, 1.00, 1.50 and 2.00 ml of 1000 μg ml^{-1} acetaminophen standard solution.

Procedure for paracetamol tablet samples

Twenty tablets of paracetamol were weighed and then powdered. A 0.1 g of powdered tablets was weighed accurately and placed in a 250 ml conical flask. A 70 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 a 100 ml volumetric flask. The filtrate was made up to the volume. A 8 ml and a 3 aliquot of sample solutions was pipetted into a 100 ml volumetric flasks and made up to volume with 0.1 mol L^{-1} phosphate buffer pH 7.0 for the direct calibration method and the standard addition method, respectively. All the commercial samples of paracetamol tablets were produced in Thailand.

RESULTS AND DISCUSSION

Effect of parameters

The peak currents were examined as a function of the step potential and modulation amplitude. A step potential of 0.002 V and a modulation amplitude of 0.05 V were selected for the rest of the experiments because at these values the 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 -1.00 V to +1.20 V. A nitrogen gas purge time of 180 seconds was used in subsequent work for the purpose of stirring.

The number of electrons involved in the oxidation of acetaminophen

The anodic peak potential, Ep,a from voltammograms of acetaminophen was measured at various pH of the media. A linear relationship was found between Ep,a and pH over the pH range of 3-11. It was found that Ep,a (V vs. Ag/AgCl) = -0.0309pH + 0.7169 (r = 0.991) with a slope of -0.0309 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 the earlier fluorimetric work (Oztunc, 1982), 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 0.1 mol L^{-1} phosphate buffer.

Calibration curve, precision, recovery and detection limit

The relationship between concentration and peak height anodic current was linear from 0 to 300 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 = 0.9997). For the determination of 30 μg ml^{-1} of acetaminophen, the coefficient of variation was 1.44% based on 15 results and the recovery from the standard addition experiments was 99.43% based on 5 results. The detection limit was 0.15 μg ml^{-1}.

Sample analysis

The contents 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 differential pulse method and the reference method. In addition, the results agreed well with the manufacturers stated values. The close agreement found between the differential pulse voltammetric method and the reference method confirmed the

Table 1 Assay of acetaminophen in paracetamol tablet samples.

Sample	Declared acetaminophen content per tablet (mg)	Acetaminophen found by calibration curve, differential pulse* (mg)	USP XXII official method by calibration curve* (mg)	Acetaminophen found by standard addition, differential pulse* (mg)	USP XXII official method by standard addition* (mg)
“Daga” Hoescht	500.0	497.0±2.8	499.2±2.4	498.3±1.3	499.2±1.8
“Paraceamol” Thai Gov. Pharma.	500.0	496.9±2.2	499.6±2.7	498.9±1.0	499.4±2.1
“Sara” Nakorn Patana	500.0	497.3±2.5	499.2±2.2	499.1±1.6	499.5±2.5
“Tylenol” OLIC(Thai)	500.0	498.2±2.8	499.1±2.9	499.1±2.2	499.5±1.6

*mean ± 95% confidence for five replicates

absence of any effects from the small amounts of excipients present.

CONCLUSION

A differential pulse 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.

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