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ELECTROCHEMICAL CHARACTERISTICS AND ANALYTICAL APPLICATIONS OF HEXADECYLMETHANESULFONATE-MODIFIED GLASSY CARBON ELECTRODES

NAMAL PRIYANTHA* and HARSHA EKANAYAKE
Department of Chemistry, University of Peradeniya, Peradeniya

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Abstract: Paracetamol and ascorbic acid are two extensively used drugs, and catechol is a neurotransmitter present in the human body. Although these substances are electrochemically active on the bare glassy carbon (GC) electrode within the cyclic voltammetric window of +1.0 V to -0.4 V, amperometric detection at bare GC electrodes does not yield accurate results due to high noise. Hexadecylmethanesulfonate (HDMS)-modified GC electrodes produce much improved signal-to-noise characteristics toward amperometric detection together with enhanced stability. Although sensitivity is little decreased due to modification with nonelectroactive HDMS, lower detection limit in the range of 10^{-4} mol dm^{-3} is achieved with the modified electrode. Hence, HDMS-modified GC electrodes can be employed to quantify the active ingredient in Paracetamol tablets.

Key wors: ascorbic acid, catechol, electrochemical detection, Hexadecylmethanesulfonate, modified electrodes, Paracetamol.

INTRODUCTION

The analysis of clinically important substances, mostly drugs, due to their significance in life, is an active area of research. However, the available techniques for the analysis of clinical substances have several drawbacks. For instance, colorimetric methods are limited to light sensitive compounds and gas chromatography for volatile substances. On the other hand, detection of these substances by gas/liquid chromatography is complex and expensive.[1,2] Therefore, the search for simple, economical and sensitive alternative techniques is a necessity. In this regard, electrochemical methods have gained attraction during the past two decades as they offer many advantages over other techniques. Consequently, electroanalytical methods such as voltammetry,[3,4] amperometry,[5,6] potentiometry, and chromatographic analysis coupled with electrochemical detection[8-10] are widely used for the determination of clinically significant substances.

Bare electrodes create many undesirable problems including unpredictable surface reactivity, interferences from the surface active or electroactive impurities and other ill-defined surface processes, many of which can be overcome by chemical modification.[11] Among different types of modifiers, electroactive modifiers act as a medium to transfer electrons between the electrode and solution, and hence they

* Corresponding author

find many applications in analytical chemistry.[12] More interestingly, some electroactive modifiers provide excellent electrocatalytic properties which make the analyte electroactive at a lower potential enhancing the power of electrochemical detection. The use of metalloporphyrin and metallophthalocyanine modified electrodes for catalytic reduction/oxidation of oxygen,[13] nitrogen oxides,[14] organohalides[15] and amino acids[16] have already been successfully attempted.

Electroinactive modifiers, on the other hand, interact with analyte molecules and alter chemical reactions, or alternatively, they act as a new phase on the conducting phase of the electrode. For instance, coatings prepared by a copolymer of styrene and maleic anhydride have been used to improve the analytical utility of GC electrodes.[17] Additionally, polymeric membranes in which analyte specific substances are incorporated have been employed in potentiometric determination of drugs.[18,19] The use of ion exchangers such as nafion and other ionomeric polymers, and neutral carriers on electrode surfaces to improve selectivity of electrochemical detection has become another attractive application in the area of chemically modified electrodes.[20] Surfactant incorporated electrode coatings have also found application in analytical chemistry, and such coatings have already been effectively used for the detection of ascorbic acid.[21] Nevertheless, the use of surfactant modified electrodes for pharmaceutical/clinical analysis has not yet become a common practice.

It is the aim of this research to investigate the mode of mass transfer and diffusion characteristics of GC electrodes modified with hexadecylmethanesulfonate (HDMS), an electroinactive substance. Novel analytical aspects of such modified electrodes, especially amperometric detection of clinically significant substances, are also reported. The validity of the proposed detection methodology is confirmed by successful analysis of commercial drug samples of Paracetamol.

METHODS AND MATERIALS

Materials: Hexadecylmethanesulfonate (HDMS), CH_3-$(CH_2)_{15}$-SO_3CH_3, was purchased from Aldrich Chemicals and used as received. The solvent used for HDMS was predistilled dichloromethane (BDH). Paracetamol standards were obtained from the State Pharmaceuticals Manufacturing Corporation, Sri Lanka, and catechol and ascorbic acid standards from BDH, England and Surechem, England, respectively. Commercial drug samples containing Paracetamol were purchased from local drug stores. The supporting electrolyte was 0.1 mol dm^{-3} NaCl, prepared in distilled water, and the volume of the electrochemical cell was 25.0 cm^3.

Instrumentation: A three electrode potentiostatic circuit, consisting of a glassy carbon (GC) working, saturated calomel (SCE) reference and a platinum wire auxiliary electrode, was used for all experiments. An Oxford Instruments Potentiostat and a YEW Instruments Model 3022 X-Y recorder were used for all measurements. All potentials were recorded with respect to SCE.

Preparation of Modified Electrodes: The coating solution of $1x10^{-3}$ mol dm^{-3} HDMS was prepared by dissolving the pure solid in predistilled dichloromethane.

The GC electrode was cleaned by polishing with alumina slurry and rinsing with distilled water, and was allowed to air dry. Then, a few drops of the coating solution were evaporated on the electrode surface. The electrode was kept in the electrolyte solution for at least 20 minutes to equilibrate before each experiment. Such prepared electrodes gave reproducible results, and the stability of the coating was fairly high.

Commercial Drug Analysis: Ten tablets of each commercial brand were selected randomly and crushed well to a uniform powder. A known weight of the powdered sample was dissolved in the electrolyte and filtered to prepare the analyte solution. A fixed volume of this solution was injected into the electrochemical cell and the corresponding amperometric current was measured. The number of trials was varied depending on the reproducibility of amperometric responses. The concentration of the active ingredient in the drug was determined with the aid of an amperometric calibration curve, which was constructed using standards. The percentage of the active ingredient of each brand, determined amperometrically, was compared with the reported values.

RESULTS AND DISCUSSION

Paracetamol analysis

Cyclic voltammetric experiments of Paracetamol standards conducted in aqueous medium at bare GC electrodes show a single oxidation peak at + 0.6 V (Figure 1a). Reversible electrochemistry is not observed as expected due to the large molecular size of the analyte. The scan rate dependence experiments carried out with $5.0x10^{-3}$ mol dm^{-3} Paracetamol solution conclude that the mode of mass transfer is mainly due to diffusion as the slope of log i_p vs. log Ov plot, where i_p is the peak current and Ov is the scan rate, is approximately 0.5. The concentration dependence of cyclic voltammetric peak current at the peak potential revealed the analytical utility of the bare GC electrode for detection of Paracetamol. The limit of detection can be decreased by employing amperometric procedures as they are more sensitive than cyclic voltammetry. However, amperometric responses of Paracetamol at bare GC electrodes are accompanied by high noise which becomes more significant as the concentration of the analyte is increased (Figure 2a). Change in the applied potential does not overcome this problem. This is probably due to the adsorption of the analyte or corresponding reaction products on the GC electrode, which is a common restriction associated with organic substances as reported by many researchers.[22] Consequently, amperometric responses of bare GC electrodes result in low and unpredictable signal-to-noise ratios, which do not lead to precise results.

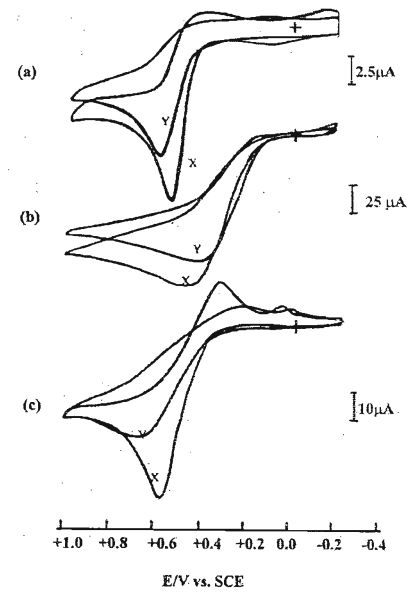

Figure 1: Cyclic voltammograms of $1.0x10^{-3}$ mol dm^{-3} solutions of (a) Paracetamol (b) Ascorbic acid (c) Catechol in 0.1 mol dm^{-3} NaCl supporting electrolyte at a scan rate of 50 mV s^{-1} under N_2 saturated. (X) Bare GC response (Y) HDMS modified GC response.

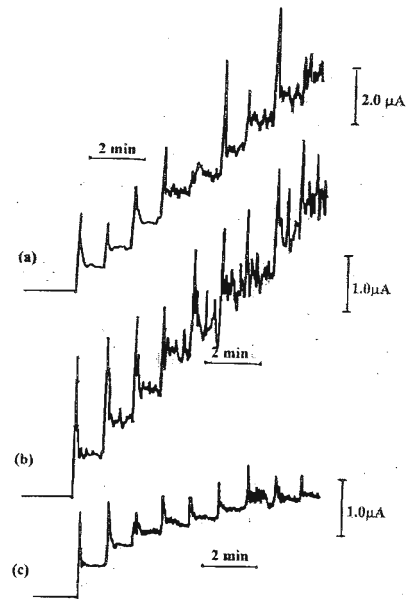

Figure 2: Amperometric responses at bare GC electrode under N_2 saturated (a) Paracetamol at +0.55 V (b) Ascorbic acid at +0.30 V (c) Catechol at +0.50 V. Supporting electrolyte 0.1 mol dm^{-3} NaCl.

Incorporation of an electrochemically inert coating on GC electrodes would prevent direct adsorption of the analyte or its reaction products on the electrode surface, because such coatings behave as a new phase which acts as a barrier for direct adsorption. Such inert coatings should be sufficiently polar or conductive enough to allow charge transfer reactions of the analyte species at the electrode surface. They should also have nonpolar properties to keep the coating stable in the aqueous medium without appreciable dissolution. Hexadecylemethanesulfonate (HDMS) is a good compromise in this regard as it possesses both polar (sulfonate) and nonpolar (long hydrocarbon chain) properties.

The use of HDMS coatings decreases the background current of GC electrodes, which indicates that the structure of the electrode surface is less sensitive to the changes in the applied potential. This results in a smaller nonfaradaic current, which favours the increase in signal-to-noise ratios in amperometric detection. Similar substances have already been used in an attempt to decrease high background currents of electrodes modified by conducting polymers.[21]

As the HDMS layer acts as a new phase, the mode of mass transfer of the analyte species towards the electrode surface may be altered. The concentration gradient of the analyte through the HDMS layer would be less than that through the electrolyte medium resulting in a lower diffusion coefficient. A percent decrease of 18% is calculated by scan rate dependence experiments at a constant bulk concentration[23] assuming that the mechanism of the charge transfer reaction of Paracetamol and the effective surface area of the electrode are unchanged during surface modification. The slope of log i_p vs. log Ov plot for Paracetamol at the modified electrode is not changed significantly as compared to the slope at the bare electrode supporting this assumption (Figure 3). The small shift of the voltammetric peak for Paracetamol at the modified electrode towards the positive potential direction as compared to that at the bare electrode confirms restricted diffusion through the HDMS phase.

Amperometric responses at the modified electrode, for the same concentration range investigated with the bare electrode, were much less noisy which would improve the precision for the detection of Paracetamol (Figure 4a). The amperometric detection procedure for Paracetamol at the HDMS-modified electrode should however be optimised with respect to the coating thickness and the applied potential, as the quality of an amperogram is dependent on these parameters. The optimum potential of operation among the potentials attempted in the vicinity of the cyclic voltammetric peak of Paracetamol is determined to be +0.55 V at the modified electrode. The sensitivity and the shape of amperometric calibration curves obtained at +0.55 V with HDMS coatings of different thicknesses (Figure 5) indicate that the optimum thickness is obtained with two drops. The minimum detection limit for this analysis is estimated to be 2.4×10^{-4} mol dm^{-3} based on the signal-to-noise ratio of 3. This level of detection is adequate in drug analysis as the level of the active ingredient in

Paracetamol preparations is probably above the minimum level of detection of the proposed amperometric method.

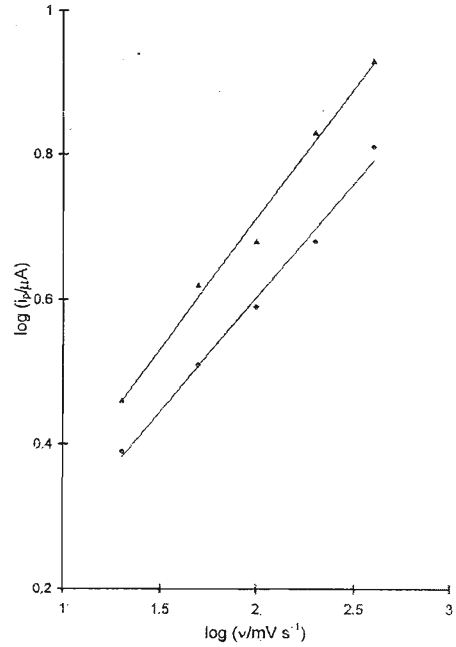

Figure 3 : A plot of log (i_p/μA) vs. log (v/mV s^{-1}) for 1.0x10^{-3} mol dm^{-3} Paracetamol solution in 0.1 mol dm^{-3} NaCl at (▲) bare (◆) HDMS modified GC electrode.

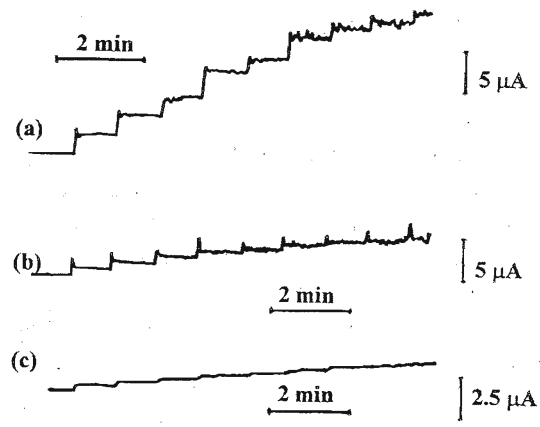

Figure 4 : Amperometric responses at the HDMS modified electrode under N_2 saturated (a) Paracetamol at +0.55 V (b) Ascorbic acid at +0.40 V (c) Catechol at +0.55 V. Supporting electrolyte 0.1 mol dm^{-3} NaCl.

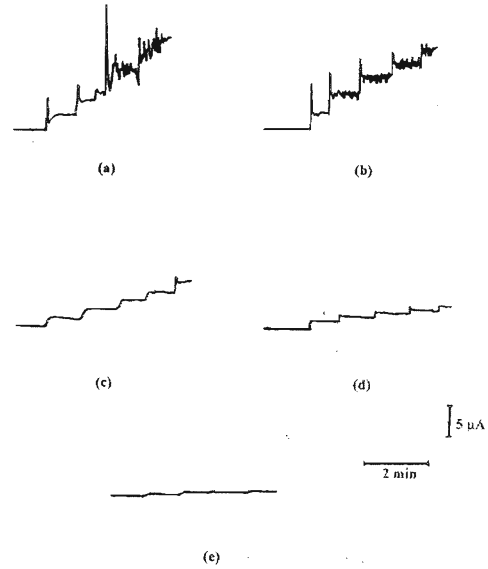

Figure 5: Effect of thickness of HDMS layers on sensitivity of amperometric detection of Paracetamol. Coatings were prepared with (a) one drop (b) two drops (c) three drops (d) four drops (e) five drops.

Analysis of Paracetamol tablets available at drug stores under different trade names (Panadol, Setamol, Fepanil, Calpol, etc.) using the proposed amperometric detection procedure resulted in the values shown in Table 1. These results are in a good agreement with the reported value of 84% active ingredient at 90% confidence level.[24]

Table 1: Amount of the active ingredient, Paracetamol, with the corresponding standard deviation (for five trials), present in different brands of drugs available in the local market.

Brand	Percent Paracetamol
Panadol	86 ± 05
Setamol	78 ± 07
Panadol caplet	86 ± 00
Paracetamol B.P.	86 ± 05
Fepanil	78 ± 06
Calpol	80 ± 10

Ascorbic acid analysis

Ascorbic acid is oxidized at the potential of +0.45 V at the bare GC electrode (Figure 1b). Cyclic voltammetric detection would not be practicable for the detection of this analyte due to less sensitivity. Further, amperometric detection of the analyte is difficult at bare electrodes due to high noise. Although the magnitude of cyclic voltammetric response of ascorbic acid at the HDMS-modified electrode was less than that at the bare electrode (Figure 1b) due to the reasons explained in the previous section, amperograms were less noisy, suggesting more precise detection at the modified electrode. Figure 4b shows the amperometric response of ascorbic acid under optimised conditions of +0.40 V operational potential and a two-drop coating.

Catechol analysis

Catechol shows many electrochemical features at bare GC electrode in the potential range of +1.0 V and -0.2 V. Nevertheless, unpredictable reactivity has been a common problem in catechol detection at bare electrodes.[17] The major oxidation peak is centered at +0.6 V while two reduction peaks appear at +0.3 V and +0.05 V, respectively (Figure 1c). Similar cyclic voltammetric behaviour is seen at the HDMS modified glassy carbon electrodes with decreased intensity of all peaks (Figure 1c). Concentration dependence of catechol at the HDMS modified GC electrode indicates the possibility of such modified electrodes as a sensor for catechol. Electrochemical detection of catechol at other types of modified electrodes to avoid complications associated with bare surfaces has already been reported.[25]

Amperometric responses at the modified electrode at an optimum potential of +0.55 V were less noisy (Figure 4c) and reproducible as observed for the other two analytes. Such procedures can easily be adopted for the detection of catechol in clinical samples.

Hexadecylmethanesulfonate (HDMS)-modified glassy carbon electrodes improve the amperometric responses of ascorbic acid, catechol and Paracetamol, which are noisy at bare electrodes. Such modified electrodes show a fair stability and enhanced reproducibility despite restricted diffusion. The lower detection limit of the modified electrode for detection of ascorbic acid is 1.2×10^{-4} mol dm^{-3}, while that for catechol and Paracetamol is 2.4×10^{-4} mol dm^{-3}. The experimental results are in good agreement with the reported values for Paracetamol analysis. HDMS modified glassy carbon electrodes would thus provide an alternative method for detection of such substances in pharmaceutical preparations.

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