Moroccan Journal of Chemistry

Eenhanced electrochemical sensing of Nimodipine with Sodium montmorillonite clay

A.Mohamed Sikkander[a], C. Vedhi[c], and P.Manisankar[b]*

[a]*Department of Chemistry, Velammal Engineering College, Chennai-600 066, Tamil Nadu, India*
[b]*Department of Industrial Chemistry, Alagappa University, Karaikudi-630003, Tamil Nadu, India*
[c]*Department of Chemistry, V.O Chidambaram College, Tuticorin-628008, Tamil Nadu, India*

**Corresponding author. E-mail :* pms11@rediffmail.com, pmsankarsiva@yahoo.com
Tel.: Phone: +91 4565 228836; Fax: +91 4565 225202
Recieved 29 August 2014, Revised 20 September 2014, Accepted 28 September 2014.

Abstract

Nano size surface of sodium montmorillonite was prepared via a colloidal physical approach and deposited onto glassy carbon electrodes and used as working electrode. A highly sensitive electrochemical biosensor for the detection of trace amount of calcium channel blocking drug has been designed. The cyclic voltametric behaviour of the drug was studied in media with five ranges of pH. Among the pHs studied, pH 13.0 showed good response for the drug. Differential pulse stripping voltammetry was employed and the optimum condition was arrived at. Accumulation of the substrate was ascertained from SEM analysis. A simple, sensitive and time-saving differential pulse stripping voltammetric procedure has been developed for determination of antihypertensive drug in its commercial tablet. The method was successfully applied to the determination of the drug in tablets and proved to be reliable.

Key words: Nimodipine, Electrochemical, sodium montmorillonite,DPSV,Peak Potential

Introduction

Since 1980, the utilization of Sodium montmorillonite (NaMM) has become popular in electrochemical studies. NaMM is a smectite clay with high chemical stability, good adsorption and good penetrability, thus making it suitable as an effective clay modified glassy carbon electrode. Electrochemical behavior of small redox substances incorporated into the

clay modified membrane has been studied extensively and reported [1]. Montmorillonite modified electrodes have been widely employed for the determination of trace analysis of pollutants [2-5].

Calcium, an essential chemical in the process of muscle contraction, is directly involved in the electrochemical reactions that allow muscle cells to contract as part of a regular heartbeat. Calcium is vital to maintaining good health, as it is involved in many everyday cellular processes, including gene regulation, memory and cell death. However, excessive levels of calcium can lead to arrhythmias, as well as hypertrophy, apoptosis and cardiac remodeling. By virtue of their ability to increase nitric oxide (NO) production, it is thought that calcium channel blockers (CCBs) may be involved in the inhibition of platelet aggregation [6].

Nimodipine, a dihydropyridine calcium channel antagonist, has potent vasodilatory effect on cerebral vessels and increases cerebral blood flow. Nimodipine, in high dosages (2–10 mg/kg), has been shown to improve memory retention and/or memory recall process in aged rats. Additionally, nimodipine and other calcium channel blockers have been shown to possess anticonvulsant properties and were found effective in affective illness [7]. These properties of nimodipine have often been neglected in recent literature. While protective effect of nimodipine has been reported inconclusively in focal and global cerebral ischemia–reperfusion models, there is no evidence of role of nimodipine on acute transient and long-term bilateral common carotid artery occlusion model [8]. Thus the determination of calcium channel blocker such as nimodipine with enhanced sensitivity and utilization of natural materials assume significance. This work is aimed to study the electrochemical behavior and assay of hypertension drugs at a NaMM clay modified glassy carbon electrode.

Methods and Material

CH Instruments Electrochemical Workstation (Model 760C) was employed mainly for carrying out electroanalytical studies. The stock solutions were made up in methanol/double distilled TKA-LAB purified water (80:20). For studies in aqueous methanol media, Britton Robinson buffers, 4.0, 7.0, 9.2, 0.1 mol.dm^{-3} KOH, KCl and 0.1 mol dm^{-3} H_2SO_4 were used asthe medium for the analysis. Montmorillonite KSF was purchased from Acros organics, Belgium.

Procedure

Purging and blanketing of nitrogen were done for analyte solution placed in the electrochemical cell of 15-ml capacity for 25 minutes under stirring. Then voltammograms were recorded. In order to get reproducible results, the glassy carbon electrode was pretreated in two ways: (a) Mechanical polishing over a velvet micro-cloth with an alumina suspension and (b) electrochemical treatment by applying a potential of 1.5 V for 2 seconds.

Results and Discussions

Electrochemical studies of Nimodipine

The voltammetric behavior of the calcium channel blocker drug was examined in the pH range 1.0–13.0 by recording their cyclic voltammograms. The effect of the pH on the peak current and potential is presented in Fig.1 and 2. The dependence of pH on peak current results in a maximum at pH 13.0. Since the best shape and sensitivity of the peak current was obtained at pH 13.0 for the the drug, this pH value is the most suitable one for the development of stripping voltammetric determination. Representative, cyclic voltammogram of 100 □g/mL of the drug in pH 13.0 is presented in Fig. 3. The nature of the oxidation process was studied by following the effect of the scan rate on the peak current. Both ip vs. □$^{1/2}$ and log ip vs. log □ dependencies gave linear plots (Fig.4&5), indicating diffusion- controlled process. Peak potential of both peaks shifts towards more negative values with the increase of the pH. The irreversibility of oxidation of the drug at NaMM/GCE was ascertained from the larger difference in anodic and cathodic peak potentials at all pHs in the range 1.0 to 13.0.

Differential pulse mode was employed for stripping voltammetric studies and it performed well in the determination of the drug on clay modified glassy carbon electrode. Experiments were carried to find out the best accumulation potential in the chosen pH 13.0 with solution containing 0.1 □g/mL of the drug.

The accumulation potential (E_{acc}) was varied from -05 to 0.6 V for drug at deposition time (DT) 15 seconds. It showed the maximum peak current for an accumulation potential at -0.1 V for NIMD (Fig.6). This may be due to electrostatic attraction between the protonated substrate and negatively charged working electrode. Deposition time was varied from 15 to 90 s and the differential pulse voltagrams were recorded. The maximum current response was observed at 30s for NIMD. The initial scan potential (ip) is also an important parameter like accumulation potential. The initial scan potential was varied between -0.5 and 0.3V for the drug and the maximum stripping peak current was measured maximum at -0.2 for NIMD.

The accumulation of the antihypertensive drug (NIMD) on the modified electrode surface under the optimum accumulation conditions was understood from the changes in the electrode surface before and after accumulation. SEM was employed to study the surface morphology of the accumulated drug on NaMM coated glassy carbon electrode. Morphology

of NaMM shows small uniform granular surface as previously reported [9,10]. The drug NIMD adsorbed on NaMM exhibited tide sponge like structure (Fig. 7). Because of the better accumulations, stripping leads to good results and hence stripping parameters was optimized.
The influences of pulse height, pulse width and potential scan increment were studied by varying their values and the maximum peak current conditions were found out. The range of study and optimized conditions are presented in Table 1. The optimum conditions that resulted in maximum peak current response were used to study the effect of analyte concentration.

Analytical characteristics

Differential pulse stripping voltammogram (DPSV) is a technique with a better peak shape and higher sensitivity, DPSV was employed for the determination of drug. Figure 8 shows DPSV curve of the drug (NIMD). The experimental results showed that the peak current increased with the increase in concentration of drug. In the range studied from
0.05 to 0.35 □g/mL for NIMD. The anodic peak current is linearly proportional to the concentration of the drug. A calibration plot indicating the linear dependence of peak current with concentration under optimum experimental condition that led to maximum peak current is shown in Figure 9. The limit of detection (LOD) was found to be 0.03 □g/mL for NIMD respectively. The reproducibility of the stripping signal was realized in terms of relative standard deviation for 7 identical measurements carried out at a concentration level of 0.03 □g/mL.

Proposed method for the determination of drugs in pharmaceutical samples

The pharmaceutical samples analyzed were collected from medical shops at Karaikudi, Tamilnadu, India. Various tablets having NIMD was examined for the estimation of content of drug. Stripping voltammograms of the drug at pH 13.0 was recorded under optimum conditions. The concentration of the calcium channel blocker in commercial formulations determined by the proposed method was in good agreement with the reported value of the company (Table.2).

Conclusion

The electrochemical oxidation of calcium channel blocker drug of Nimodipine at a sodium montmorillonite modified GCE was identified in buffered solutions and a validated voltammetric procedure was described for its determination. The described procedure provides a sensitive and simple approach to the determination of drug in pharmaceutical formulations. Its accuracy, reproducibility, simplicity and selectivity suggest its application in quality control analysis, clinical laboratories and pharmacokinetic studies.

References

[1] Lei, C., Wollenberger, U., Bistolas, N., Guiseppi-Elie, A., Scheller, F.W., 2002. Electron transfer of hemoglobin at electrodes modified with colloidal clay nanoparticles, Anal Bioanal Chem, 372; 235–239.

[2] Manisankar, P., Vedhi, C., Selvanathan, G., 2003. Electrochemical determination of methyl parathion using a modified electrode. Toxicological & Environmental Chemistry, 85; 233 – 241.

[3] Manisankar, P., Selvanathan, G., Vedhi, C., 2005. Utilization ofsodium montmorillonite clay-modified electrode for the determination of isoproturon and carbendazim in soil and water samples. Applied Clay Science, 29; 249-257.

[4] Manisankar, P., Selvanathan, G., Vedhi, C., 2006. Determination of pesticides using heteropolyacid montmorillonite clay-modified electrode with surfactant. Talanta, 68; 686-692

[5] Manisankar, P., Muralidharan, B., Gopu, G., Vedhi, C., 2008. Voltammetric determination of analgesics and urine using a montmorillonite modified electrode. Applied Clay Science, 42; 206-213.

[6] Sirmagül, B., Ozdener, F., Gulbas Z., Erol, K., 2007. Calcium channel blockers increase the amount of nitrite production in rabbits without decreasing the responsiveness of platelets to collagen, Clinical and Experimental Medicine, 7; 142-148.

[7] Czuczwar, S.J., Gasior, M., Janusz, W., Kleinrok, Z., 1992. Influence of flunnarizine, nicardipine and nimodipine of the anticonvulsant activity of different antiepileptic drugs in mice. Neuropharmacology, 31; 1179–83.

[8] Yanpallewar, S.U., Hota, D., Rai, S., Kumar, M., Acharya, S.B., 2004. Nimodipine attenuates biochemical, behavioral and histopathological alterations induced by acute transient and long-term bilateral common carotid occlusion in rats. Pharmacological Research, 49; 143–150.

[9] Muralidharan B. Gopu G. Vedhi C. Manisankar P. (2009). J. Appl. Electrochem., 39,1177.

[10] Mohamed Sikkander A. Vedhi C. Manisankar P(2012).*International Journal of Industrial Chemistry* , **3**:29 (6 November 2012)