Signal amplification of dopamine using lanthanum hexacyanoferrate-modified electrode

T SELVARAJU[a,b,*] and R RAMARAJ[a]

[a]Centre for Photoelectrochemistry, School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India
[b]Department of Chemistry, Karunya University, Coimbatore 641 114, India
e-mail: selvaraju@karunya.edu

Abstract. A sensitive and selective electrochemical sensor has been developed using an electroactive polynuclear lanthanum hexacyanoferrate (LaHCF) complex with counter alkali cation (Na^+) deposited on the glassy carbon (GC) electrode (GC/LaHCF). The GC/LaHCF-modified electrode is found to be an excellent transducer in mediating the oxidation of neurotransmitter molecule such as dopamine (DA) at physiological pH 7.2. Interestingly, the GC/LaHCF-modified electrode amplifies a 50-fold enhancement in the oxidation of DA signal compared to the bare GC electrode. Besides, the GC/LaHCF-modified electrode shows excellent selectivity in the voltammetric oxidation of DA in the presence of ascorbic acid (AA). Under optimal conditions, the GC/LaHCF modified electrode shows a linear relationship in DA oxidation between 0.1×10^{-6} and 1.0×10^{-6} M with the detection limit of 1×10^{-8} M (10 nM). Importantly, practical utility of the modified electrode is good in studying the real sample analysis such as dopamine hydrochloride injection assay.

1. Introduction

Prussian blue (PB) and its analogues which belong to a class of polynuclear inorganic compounds and resemble redox organic polymers and zeolitic or intercalation materials are studied extensively in various applications.[1–17] Although, transition metal hexacyanoferrate series are exploited to a greater extent, limited studies are conducted on the properties and applications of rare earth metal hexacyanoferrates, for e.g., lanthanum hexacyanoferrate, etc.[9,18,19] Lanthanum finds potential applications in hydrogen storage materials, ion-selective electrodes, chemical sensors, electrocatalytic hydrogenation of organic substrates and as a promoter to facilitate the electrochemical reactions of biological molecules.[9,10] In general, the deposition of highly stable film on the electrode surface is a major criterion in various applications.[10–17] Liu *et al.* have introduced two new PB analogues, namely zirconium hexacyanoferrate[20,21] ($K[Zr_3(OH)_6Cl_3]Fe(CN)_6$) and lanthanum hexacyanoferrate[9] ($Na^+La^{3+}[Fe^{II}(CN)_6]$) (LaHCF), in solid-state electrochemistry. It reveals that the small channels of LaHCF lattice were unable to accommodate alkali metal cations and no obvious voltammetric response was observed in the supporting electrolyte such as NaCl and poor performance in the presence of KCl.[9] Wang *et al.* have used lanthanum hexacyanoferrate-modified electrode in the determination of uric acid in the presence of AA, whereas the voltammetric response was very poor in the presence of KCl.[22] On the other hand, in the present study, LaHCF on glassy carbon (GC) electrode surface shows a very good voltammetric response in the presence of NaCl.

DA is one of the most significant catecholamines which belong to the family of excitatory chemical neurotransmitters. It plays a very important role in functioning the central nervous, cardiovascular, renal and hormonal systems, as well as drug addiction and Parkinson's disease.[23–25] DA and AA usually coexist in the human biological system and undergo electro oxidation in the same potential which results in overlapping voltammetric responses making their discrimination highly difficult.[26,27] Thus, the determination of submicromolar concentration of DA in the presence

*For correspondence

of interferences has gained much attention.[23–30] The conducting polymer incorporated metal hexacyanoferrates show poor selectivity towards DA determination.[31,32] Cobalt hexacyanoferrate-modified electrodes,[13,14,33] Th(IV)-hexacyanoferrate-modified electrodes[34] and ruthenium hexacyanoferrate-modified electrodes[35] were used to study the high concentrations of DA. Besides, nickel hexacyanoferrate,[36,37] silver hexacyanoferrate[38] and tin hexacyanoferrate-modified[39] electrodes were studied at slightly higher concentrations of DA. In the absence of inference such as AA, neodymium hexacyanoferrate-modified electrode was used to study DA.[40] To the best of our knowledge, there is no report on the electrochemical investigation of lanthanum hexacyanoferrates towards the oxidation of neurotransmitter molecule such as DA. In the present study, first, the preparation and electrochemical characterization of LaHCF-modified GC electrode in the presence of NaCl are highlighted. Secondly, the signal amplification towards DA oxidation is justified and the estimation of DA in the presence of AA, is discussed, at the GC/LaHCF-modified electrode. Finally, a simple and robust amperometric read-out is tabulated for real sample analysis such as dopamine hydrochloride injection solution using this modified electrode.

2. Experimental

Lanthanum chloride, dopamine hydrochloride, ascorbic acid and potassium hexacyanoferrate (Merck) were used without any further purification. All other chemicals were of analytical grade and used as received. Freshly prepared solutions of DA and AA were used in all experiments. Phosphate buffer solution (0.1 M, pH 7.2) was prepared using $Na_2HPO_4.12H_2O$ and $NaH_2PO_4.2H_2O$ (Merck) stock solutions. All solutions were prepared using doubly distilled water.

Electrochemical experiments were performed with an EG&G PAR model 283 potentiostat/galvanostat controlled by Echem software loaded personal computer. The electrochemical measurements were carried out with a two-compartment three-electrode cell, containing platinum wire as a counter electrode, standard calomel electrode (SCE) as a reference electrode and glassy carbon (CH Instruments Inc.) or modified GC electrode as a working electrode ($0.07\,cm^2$). Prior to each experiment, the GC electrode was polished with the slurries of 0.3 and 0.05 μm alumina to a mirror finish and rinsed using doubly distilled water. Then, the electrodes were ultrasonicated in doubly distilled water for about 2 min. Finally, the electrode was activated by cycling between –0.2 and 0.8 V in 0.1 M KCl at a scan

rate of $50\,mV\,s^{-1}$ in order to get a stable cyclic voltammogram. In this study, all the potentials were quoted against SCE.

The GC/LaHCF-modified electrode was prepared using freshly prepared equimolar mixture of 10 mM $LaCl_3$ and 10 mM $K_3Fe(CN)_6$ solution containing 0.3 M NaCl by potential cycling between 0.8 V and –0.2 V at a scan rate of $50\,mV\,s^{-1}$ for 20 cycles. The LaHCF was found to grow on the surface of the GC electrode with respect to a number of potential cycles. Finally, the electrode was washed with distilled water and used in voltammetric applications.

3. Results and discussion

3.1 *Electrosynthesis of LaHCF on GC electrode*

The GC/LaHCF-modified electrode was prepared by cycling the potential between 0.8 V and –0.2 V at a scan rate of $50\,mV\,s^{-1}$ in 0.3 M NaCl solution containing an equimolar mixture of 10 mM $LaCl_3$ and 10 mM $K_3Fe(CN)_6$. Figure 1 shows the continuous cyclic voltammograms recorded during LaHCF film formation on the GC electrode. During electrosynthesis, the redox peak current was decreased gradually with respect to potential cycling (figure 1). Thus, in the electrosynthesis process, it is understood that there are two steps involved in the generation of LaHCF on the electrode surface (eqs 1 and 2). The first step is the electroreduction of $[Fe^{III}(CN)_6]^{3-}$ to $[Fe^{II}(CN)_6]^{4-}$. Instantaneously, the reduced $[Fe(CN)_6]^{4-}$ forms a

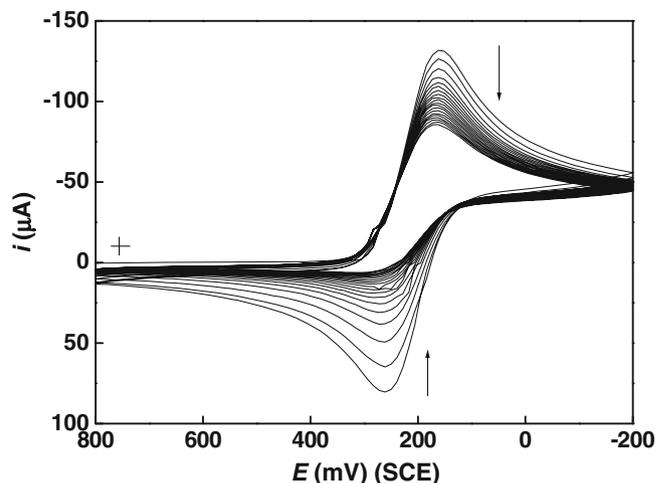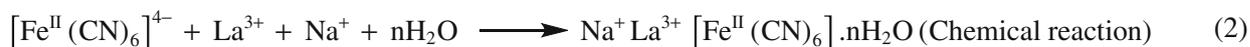**Figure 1.** Continuous CVs recorded during electrosynthesis of LaHCF on GC electrode using 10 mM $LaCl_3$, 10 mM $K_3Fe(CN)_6$ and 0.3 M NaCl. Number of cycles = 20. Scan rate = $50\,mV\,s^{-1}$.

complex with La^{3+} ion, which is a chemical reaction that firmly deposited as sodium lanthanum hexacyano-ferrate(II) ($Na^+La^{3+}[Fe^{II}(CN)_6]$) on the surface of the GC electrode.[9]

$$\left[Fe^{III}(CN)_6\right]^{3-} + e^- \longrightarrow \left[Fe^{II}(CN)_6\right]^{4-} \text{ (Electrochemical reaction)} \tag{1}$$

$$\left[Fe^{II}(CN)_6\right]^{4-} + La^{3+} + Na^+ + nH_2O \longrightarrow Na^+La^{3+}\left[Fe^{II}(CN)_6\right].nH_2O \text{ (Chemical reaction)} \tag{2}$$

Voltammetric characteristics of the LaHCF film formation process at the electrode surface are different from the electrochemically deposited transition metal hexacyanoferrates such as cobalt hexacyanoferrate,[41] nickel hexacyanoferrate[41] and the mixed hexacyanoferrates of nickel and palladium.[33,42,43] In the electrosynthesis process of transition metal hexacyanoferrates, the peak current increases with an increase in the number of potential cycles and attained saturation; whereas in the case of inner transition metal hexacyanoferrate, LaHCF, the behaviour is quite different. Here, the redox peak current decreases which is due to electrochemical reaction followed by a chemical reaction (eqs 1 and 2) which takes place during LaHCF film formation. Accordingly, the free $[Fe^{III}(CN)_6]^{3-}$ hardly gets deposited on the electrode surface, whereas it tends to reduce as $[Fe^{II}(CN)_6]^{4-}$, and besides in the presence of La^{3+}, it forms LaHCF complex on the electrode surface (eqs 1 and 2). During LaHCF formation, these two-step reactions lead to a gradual decrease in the redox peak current. In order to form a stable LaHCF film with good transport and conducting properties, the electrosynthesis process requires a relatively high concentration of precursors such as $LaCl_3$ ($\sim$10 mM) and $K_3Fe(CN)_6$ ($\sim$10 mM). It is well-known that the film formation of transition metal hexacyanoferrates on the electrode surface is rapid in a solution of low concentration ($\sim$0.5 mM).[33,41–43] On the other hand, our experimental results indicate that the LaHCF film formation was observed at relatively high concentrations of precursors. The observed result is justified by eqs 1 and 2.

3.2 *Electrochemical characterization of GC/LaHCF electrode*

Cyclic voltammograms of the GC/LaHCF electrode were recorded in the presence of a solution containing 0.3 M NaCl and 0.1 M HCl at various scan rates (figure 2). The observed $E_{1/2}$ value (0.31 V) and the peak separation potential ($\Delta E_p = 60$ mV), are almost independent of scan rates in the range of 10–100 mV s^{-1}. Anodic and cathodic peak currents are increase linearly

with the square root of scan rate (figure 3 inset) indicating that diffusion-controlled electron transfer process is observed at the LaHCF-modified electrode. It is established that the simultaneous motion of counter cations such as Na^+, K^+, etc., occur to attain an electroneutrality during the electrochemical reaction of metal hexacyanoferrates.[9] Eventually, the formal potential of LaHCF is noted as more negative than that of the transition metal hexacyanoferrates such as cobalt and nickel hexacyanoferrates.[41]

3.3 *Signal amplification of DA oxidation at GC/LaHCF modified electrode*

Figure 3 shows the cyclic voltammograms recorded for the GC/LaHCF electrode in 0.1 M phosphate buffer (pH 7.2) at a scan rate of 50 mV s^{-1} in the absence and presence of 0.1 M NaCl. Redox behaviour of the GC/LaHCF-modified electrode gets improved in the presence of Na^+ ions with an $E_{1/2}$ at 0.2 V. To
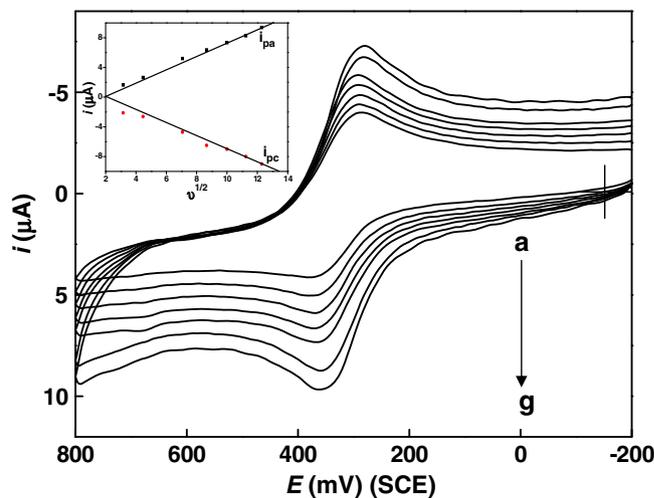
Figure 2. CVs obtained at GC/LaHCF electrode in a mixture of 0.3 M NaCl and 0.1 M HCl at various scan rates. The scan rates are: $a = 10$, $b = 20$, $c = 50$, $d = 75$, $e = 100$, $f = 125$ and $g = 150$ mV s^{-1}. The inset shows the dependence of anodic and cathodic peak currents against square root of scan rate.
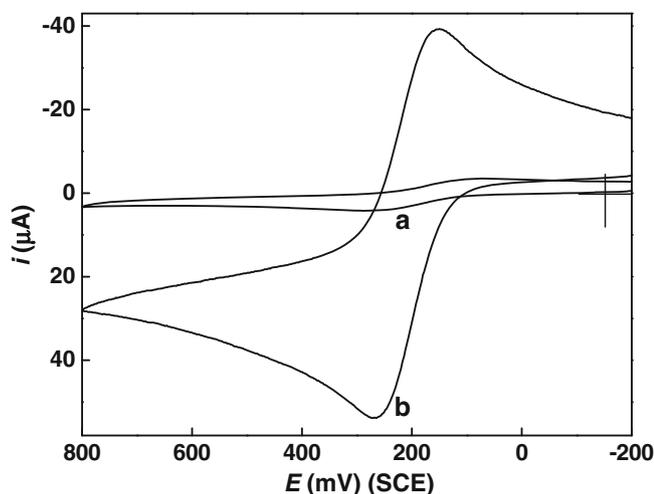
Figure 3. CVs obtained at GC/LaHCF modified electrode in 0.1 M phosphate buffer in the absence (**a**) and presence (**b**) of 0.1 M NaCl. Scan rate = 50 mV s^{-1}.
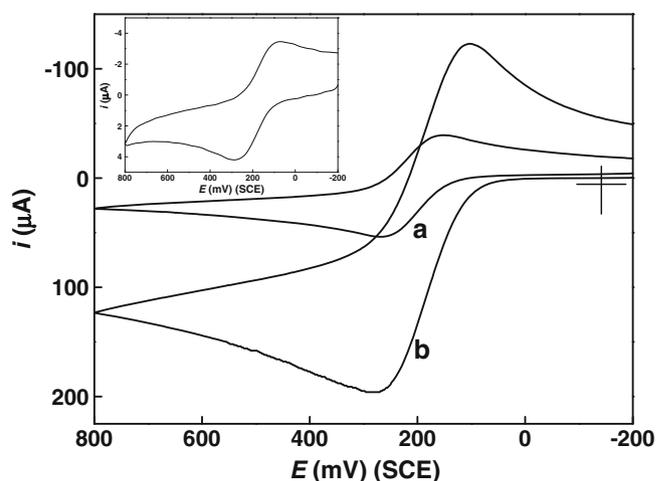

Figure 4. CVs obtained at GC/LaHCF electrode in 0.1 M phosphate buffer containing 0.1 M NaCl in the absence (**a**) and presence (**b**) of 10 μM DA. Inset shows the CV of 10 μM DA at bare GC electrode in 0.1 M phosphate buffer containing 0.1 M NaCl. Scan rate = 50 mV s^{-1}.

the best of our knowledge, this type of excellent quasi-reversible cyclic voltammetric response is not yet reported for lanthanum hexacyanoferrate-modified electrode. Influence of anions on the electroactivity of metal hexacyanoferrates has been described elsewhere.[44,45] However, it seems implausible that adding chlorides might cause the observed massive increase in the peak current. In the present study, the reduced form of LaHCF could amplify the oxidation signal of biologically important neurotransmitter molecule such as DA. To investigate the electron-mediating activity of the GC/LaHCF-modified electrode, DA oxidation was studied. Figure 4 shows cyclic voltammograms recorded for the GC/LaHCF-modified electrode both in the absence and presence of DA. A stupendous increase in the oxidation peak current is observed for DA at the GC/LaHCF electrode (figure 4b) compared to the absence of DA (figure 4a). On the other hand, a significant peak current is not observed for DA at the bare GC electrode as shown in figure 4(inset). Thus a 50-fold enhancement in the peak current towards DA oxidation is observed at the LaHCF-modified electrode compared to the bare GC electrode. It means that the promotional effect of LaHCF is the basis for the high electron facilitating activity towards DA oxidation. Schematic representation of DA oxidation by the LaHCF ($Na^+La^{3+}[Fe^{II}(CN)_6]$)-modified electrode is shown in figure 5. A similar kind of observation was recorded at the superoxide dismutases-modified electrode.[46]

Figure 6 shows the differential pulse voltammograms (DPV) recorded for different concentrations of
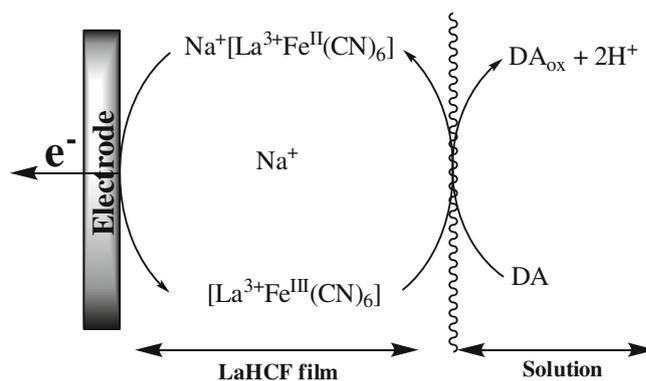

Figure 5. Schematic representation of electrooxidation of DA at the GC/LAHCF electrode.

DA at the GC/LaHCF electrode. The DPV peaks are well-defined and the peak currents are proportional to the [DA] and increase linearly with increasing DA concentration (figure 6 inset) with a correlation coefficient of 0.997. When compared to bare GC electrode, the DPV shows a significant amplification in the anodic peak current due to DA oxidation at the GC/LaHCF electrode. Detection limit of DA at the GC/LaHCF-modified electrode is calculated as 10 nM at a signal-to-noise ratio of 3. After 10 repetitive cycles, no significant losses in the anodic peak current are observed for DA oxidation at the modified electrode.

3.4 Selective oxidation of DA in the presence of AA

The modified electrode should possess selectivity towards DA oxidation in the presence of interferences
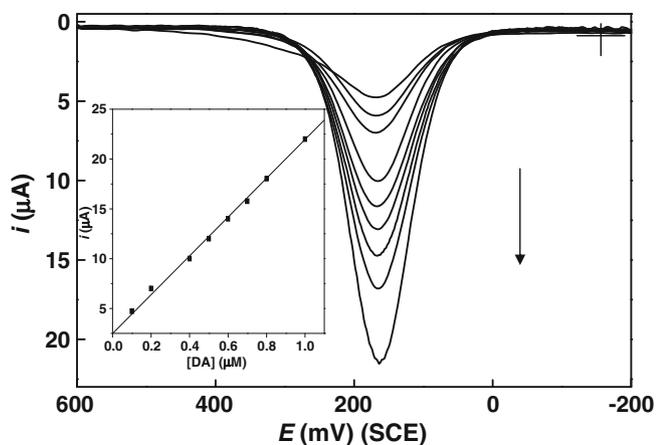
Figure 6. DPVs obtained at GC/LaHCF electrode in 0.1 M phosphate buffer containing 0.1 M NaCl in the presence of different [DA]. Scan rate = 5 mV s^{-1}. [DA] = 0, 0.1, 0.2, 0.4, 0.5, 0.6, 0.7, 0.8 and 1.0 μM. Inset depicts the plot of peak current *vs.* [DA].
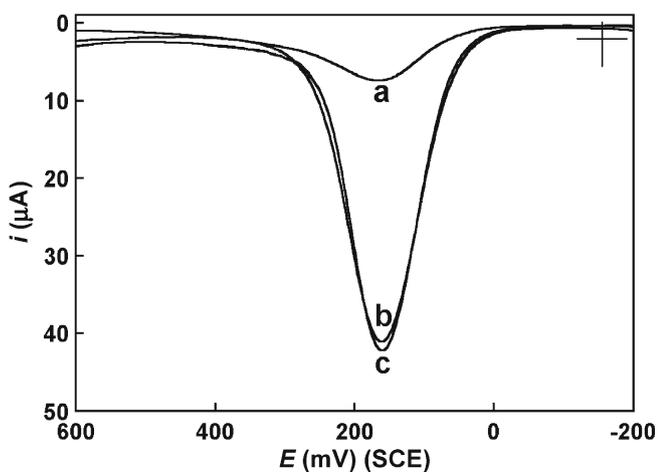

Figure 7. DPVs obtained at GC/LaHCF electrode in 0.1 M phosphate buffer containing 0.1 M NaCl (**a**) in the absence of DA and AA, (**b**) 5 μM DA in the presence of 0.1 mM AA and (**c**) 5 μM DA in the absence of AA. Scan rate = 5 mV s^{-1}.

such as AA, nitrite, nitrate and other neurotransmitters metabolites. Owing to the higher concentrations, AA is an important interfering species in the biological systems. One useful strategy to eliminate AA, involves electrostatic repulsion by the anionic polymer, particularly Nafion (Nf) at the electrode surface due to its permselective behaviour.[29,30] In the present study, in order to show selectivity towards DA oxidation at the modified electrode surface, the voltammetric behaviour was investigated in the presence of AA. Figure 7(a) shows the DPV recorded at the LaHCF-modified electrode in a solution containing 0.1 M phosphate buffer and 0.1 M NaCl. Figure 7(b) and (c) show the DPVs for DA oxidation in the presence (curve b) and in the absence of AA (curve c) at GC/LAHCF electrode. In the presence of AA, there is no significant change in the DA oxidation (figure 7b). Furthermore, LaHCF-modified electrode in the presence of 0.1 M NaCl would be an effective barrier towards AA electroxidation and thereby selective oxidation of DA is achieved.

3.5 *Analytical application*

Analytical application of LaHCF-modified electrode in the determination of DA is being extended to study real sample analysis such as dopamine hydrochloride injection solution (DHI). Exact concentration of DA in DHI injection solution is determined by the standard addition method (spike method) using GC/LaHCF-modified electrode and the results are summarized in table 1. Under the optimum conditions chosen, the DPV peak currents are linearly related to [DA] over the concentration range between 5.0×10^{-8} and 5×10^{-6} M with a correlation coefficient of 0.992 (figure not shown). A detection limit of 10 nM is estimated at a signal-to-noise ratio of 3. The DA is repeatedly determined with duplicate samples and the relative standard deviation is found to be 7.5%.

Table 1. Estimation of dopamine in DHI solution using GC/LaHCF-modified electrode.[a]

Sample	DA content DHI (μM)	DA found[b] (μM) ($n = 3$)	DA spike (μM)	DA found[b] (μM)	Mean recovery (%) ± S.D. ($n = 3$)
1	10	9.6	10	9.8	98.0 ± 2.1
2	10	9.0	10	9.2	92.2 ± 8.8
3	10	9.2	10	9.4	94.4 ± 6.5

[a]Potential scan rate was 5 mV s^{-1} for DPV and other conditions were as given in figure 6
[b]Average values of three determinations

4. Conclusion

On GC electrode, the rare earth metal hexacyanoferrate, LaHCF ($Na^+La^{3+}[Fe^{II}(CN)_6]$), has been successfully electrodeposited, which exhibits a diffusion controlled reaction mechanism. The highlight of this study is the promotion of electron mediation activity towards DA oxidation in phosphate buffer containing 0.1 M NaCl at the GC/LaHCF-modified electrode. Importantly, in the presence of interference such as AA, selective oxidation of DA is achieved in phosphate buffer containing NaCl. Thus, the GC/LaHCF-modified electrode is found to be an excellent and satisfactory electrochemical read-out method for the neurotransmitter molecule such as DA with a detection limit in the submicromolar range.

Acknowledgements

References

1. Scholz F and Meyer B 1998 In *Electroanalytical chemistry* A J Bard and I Rubinstein (eds) (New York: Marcel Dekker) vol. 20
2. Itaya K, Uchida I and Neff V D 1986 *Acc. Chem. Res.* **19** 162
3. Widmann A, Kahlert H and Prelevic I P 2002 *Inorg. Chem.* **41** 5706
4. de Tacconi N R, Rajeshwar K and Lezna R O 2003 *Chem. Mater.* **15** 3046
5. Ricci F and Palleschi G 2005 *Biosens. Bioelectron.* **21** 389
6. Zen J-M, Kumar A S and Tsai D M 2003 *Electroanalysis* **15** 1073
7. Vittal R and Gomathi H 2002 *J. Phys. Chem.* **B106** 10135
8. Lezna R O, Romagnoli R and de Taccon N R 2002 *J. Phys. Chem.* **B106** 3612
9. Liu S Q and Chen H Y 2002 *J. Electroanal. Chem.* **528** 190 and references cited therein
10. Druten G M R V, Labbe E and Boncour V P 2000 *J. Electroanal. Chem.* **487** 31 and references cited therein
11. Jiang H-J, Huang X-H and Wang X-F 2003 *J. Electroanal. Chem.* **545** 83
12. Cai C X, Xue K H and Xu S M 2000 *J. Electroanal Chem.* **486** 111
13. Xun Z Y, Cai C X and Xing W 2003 *J. Electroanal. Chem.* **545** 19
14. Chen S M and Peng K T 2003 *J. Electroanal. Chem.* **547** 179
15. Golabi S M and Noor-Mohammadi F 1998 *J. Solidstate Electrochem.* **2** 30
16. Cataldi T R I, de Benedetto G and Bianchini A 1999 *J. Electroanal. Chem.* **471** 42
17. Ohkoshi S, Fujishima A and Hashimoto K 1998 *J. Am. Chem. Soc.* **120** 5349
18. Wu P, Lu S and Cai C X 2004 *J. Electroanal. Chem.* **569** 143
19. Wu P and Cai C X 2005 *Chin. J. Chem.* **V23** 127
20. Liu S Q, Chen Y and Chen H Y 2001 *J. Electroanal. Chem.* **502** 197
21. Liu S Q, Chen Y and Chen H Y 2002 *Electroanalysis* **14** 116
22. Wang G, Meng J, Liu H, Jiao S, Zhang W, Chen D and Fang B 2008 *Electrochim. Acta* **53** 2837
23. Gonon F, Buda M and Cespuglio R 1980 *Nature* **286** 902
24. Adams R N 1976 *Anal. Chem.* **48** 1128A
25. Sternson A W, Mccreery R and Feinberg B 1973 *J. Electroanal. Chem.* **46** 313
26. Zen J-M and Chen P-J 1997 *Anal. Chem.* **69** 5087
27. Selvaraju T and Ramaraj R 2003 *Electrochem. Commun.* **5** 667
28. Dayton M A, Ewing A G and Wightman R M 1980 *Anal. Chem.* **52** 2392
29. Mauritz K A and Moore R B 2004 *Chem. Rev.* **104** 4535
30. Selvaraju T and Ramaraj R 2005 *J. Electroanal. Chem.* **585** 290
31. Chen T-W, Tsai T-H and Chen S-M 2010 *ECS Trans.* **33** 141
32. Tsai T-H, Chen T-W, Chen S-M and Saraswathi R 2012 *Russ. J. Electrochem.* **48** 291
33. Xun Z-Y, Cai C-X and Lu T-H 2004 *Electroanalysis* **16** 674
34. Farhadi K, Kheiri F and Golzan M 2008 *J. Braz. Chem. Soc.* **19** 1405
35. Shervedani R K and Alinajafi-Najafabadi H A 2011 *Int. J. Electrochem.* **603135** 11pp
36. Prabakar S J R and Narayanan S S 2009 *Electroanalysis* **21** 1481
37. Mashhadizadeh M H, Yousefi T and Golikand A N 2012 *Electrochim. Acta* **59** 321
38. Noroozifar M, Khorasani-Motlagh M and Taheri A 2010 *Talanta* **80** 1657
39. Hosseinzadeh R, Sabzi R E and Ghasemlu K 2009 *Colloids Surf. B: Biointerf.* **68** 213
40. Fang B, Shen R, Zhang C, Yuan H, Yao L and Wang G 2009 *Electroanalysis* **21** 2680
41. Chen S-M 2002 *J. Electroanal. Chem.* **521** 29
42. Kulesza P J, Malik M A and Schmidt R 2000 *J. Electroanal. Chem.* **487** 57
43. Kulesza P J and Malik M A 1998 *J. Phys. Chem.* **B102** 1870
44. Malik M A, Miecznikowski K and Kulesza P 2000 *Electrochim. Acta* **45** 3777
45. Malik M A, Horanyi G and Kulesza P J 1998 *J. Electroanal. Chem.* **452** 57
46. Tian Y, Mao L, Okajima T and Ohsaka T 2004 *Anal. Chem.* **76** 4162