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A Sensitive Electrochemical Sensor for Determination of Imipramine in Urine Sample Using Carbon Ionic Liquid Electrode Modified With Montomorillonite Nanoclay

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Abstract

We used an effective electrochemical sensor for the determination of imipramine at pH 7.2 using a carbon nanocomposite electrode. The electrode has been designed by incorporation of montmorillonite nanoclay into the carbon ionic liquid electrode. The high sensitivity of 1.714 μA $(\mu M)^{-1}$, two linear calibration ranges of 0.1–2 μM and 2-40 μM, and detection limit of 19 nM were achieved. The relative standard deviations (RSDs) were 2.73% (n=7, 2 μM), 2.97% (n=4, 2 μM), respectively. Thus, this modified electrode was further applied to the determination of imipramine in urine sample.

Keywords: Carbon ionic liquid electrode, Electrochemical sensor, Imipramine, Montomorillonite Nanoclay.

1. Introduction

Imipramine (10,11-dihydro-*N*,*N*-dimethyl-5*H*-dibenz[*b*,*f*]-azepine-5-propanamine), a tricyclic antidepressant (TCA) , is one of the most commonly prescribed drugs for the treatment of psychiatric patients suffering from various forms of depression [1]. Imipramine is also given in selected cases for the treatment of nocturnal eneuresis in children. For therapy, appropriate amount of the drug is required to obtain optimum therapeutic effects, and minimize severe side-effects and toxicity [2]. Therefore selective and sensitive detection of imipramine in body fluids is preciously important. Electrochemical methods have attracted considerable attention due to their excellent sensitivity, short analysis time, simplicity and require less expensive equipment than other methods [1-7]. Recently, the application of nano materials has attracted considerable attention in electrochemical researches because of the unique properties of these materials [8]. Among these attractive

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nanomaterials, cheap and naturally occurring, readily available clay minerals are widely employed as modifier [9]. Clays are stable aluminosilicates with high cation exchange capacity, and exfoliated clay particles have a platelet shape with nanoscopic size [10]. Because of ionic exchange capacity, good catalytic support, large surface area, mechanical stability, nontoxic materials and low cost properties of clays, their application in the modification of the surface of electrodes has been considered [11]. Montmorillonite nanoclay with its inherent layered inorganic nanostructure is a member in the smectite group of clays [12,13,14] and has a high affinity for several substances (e.g., heavy metals and organic molecules) [11,13]. Clays are also mixed with carbon paste electrode (CPE) to enhance the adsorption and ion-exchange properties of the electrode [15]. Room temperature ionic liquids (RTILs) have been proposed to be very interesting and efficient pasting binder in place of non conductive organic binders for the preparation of carbon ionic liquid electrodes (CILEs) [15, 16]. CILE exhibits properties for electrochemical applications, such as low cost, ease of preparation, antifouling effect and renewable surface [17]. The interaction of ionic liquids (ILs) and clays were studied and they were applied as a suitable matrix for immobilization of different biomolecules on the surface of electrodes [7,12,18,19]. Since working with urine sample is complicated and every electrode does not respond to it, we used montmorillonite nanoclay modified carbon ionic liquid electrode, as introduced in our previous paper in order to determine imipramine in urine sample.

The results illustrate that the electrode exhibits an excellent route to the sensitive determination of imipramine. The proposed electrode is simple to prepare, reproducible, easily renewable and cost effective.

2. Experimental

2.1 Chemicals and Apparatus

Imipramine hydrochloride (10, 11-dihydro-*N*, *N*-dimethyl-5*H*-dibenz [*b*, *f*]-azepine-5-propanamine – hydrochloride), pyridine, diethyl ether, paraffin oil (Merck), montmorillonite nanoclay, graphite powder (particle size <100 mm) (Aldrich), ammonium hexafluorophosphate and iodooctane (Fluka) were used as received. All other chemicals were of analytical grade. The IL, octylpyridinium iodide, was synthesized as described elsewhere [20]. For preparing all solutions, deionized distilled water was used and Briton-Robinson buffer solution was utilized in order to study the effect of pH on the analytical signal. In addition, urine sample obtained from healthy individuals were stored frozen until assay.
Electrochemical measurements were done with a galvano potentiostat Behpajooh Co. model BHP2063+. The electrochemical cell was assembled with a conventional three-electrode system; with a saturated calomel electrode as a reference electrode (SCE) and a platinum disk as a counter electrode, and CILE (nanoclay modified carbon ionic liquid electrode (NC–CILE), carbon-paste electrode (CPE), nanoclay modified carbon paste electrode (NC-CPE)) as the working electrode. The cell was a one-compartment cell with an internal volume of 10 mL. All experiments were typically conducted at room temperature.

2.2 Electrode Preparation

CILE was prepared by hand-mixing, in a mortar, the graphite powder and IL ($[OPy]^+$ $[PF6]^-$) in a mortar with a ratio of 70/30 (w/w). A portion of the resulting paste was

packed firmly into the cavity (2.0 mm i.d.) of a Teflon holder. Note that in order to have better homogeneity in the composite and to lower background current, the electrode should be heated (e.g. by using a hair drier) to a temperature above the melting point of IL (m.p. ~ 65 ^{o}C) prior to use [15]. The electric contact was established with a copper wire contact to the carbon composite. NC-CILE was prepared in the same way as CILE with the weighed amounts of graphite powder, IL, and nanoclay (60: 30: 10, wt %), respectively. The unmodified CPE was prepared by mixing graphite powder and appropriate amount of paraffin oil with a ratio of 70/30 (w/w) graphite/ paraffin oil. The paste was packed into the cavity of a Teflon tube (2-mm diameter). NC-CPE was prepared in the same way as CPE with the weighed amount of graphite powder, nanoclay and paraffin oil (60: 10: 30, wt %).

3. Results and discussion

SEM micrographs of nanoclays (as received) and NC-CILE [7] show nanoclays are in the form of large and small aggregates, after the incorporation of nanoclays into the CILE, nanoclay particles are dispersed in the form of homogeneous nanostructures with a dimension about 30 nm. Certainly, the narrowly dispersed nanoparticles enhance the contact surface area of the clays with the solution.

The cyclic voltammograms of 0.1 mM imipramine (IMP) in 0.07 M phosphate buffer solution (pH 7.2) obtained at a potential sweep rate of 50 mVs^{-1} at CILE, NC-CILE (10%, wt %), CPE and NC-CPE (10%-wt%) are given in Figure 1. None of these electrodes show any peak in the absence of IMP (curves a, b, c, d). It can be seen that the anodic peak due to oxidation IMP at CILE (curve g) appears at about 0.65 V. At NC-CILE (curve h), the peak potential is slightly shifted to a more positive potential of 0.7 V, but, the current increased to a higher value. In comparison with CILE and NC-CILE, the peak currents are lower and the peak potentials appear at more positive potentials at CPE (curve e) and NC-CPE (curve f). The peak potentials of CILE and NC-CILE for IMP oxidation were also lower than those reported on a BDE (~0.844 V) [2], a glassy carbon electrode (GCE) (~0.800 V) [2], an ITO electrode modified by Au nanoparticles (ca. 0.884 V) [3] and a titanium dioxide-Amberlite XAD-nanoparticles modified GC paste electrode (0.833 V) [21]. It is interesting to note that an increase in faradic currents (increase in the sensitivity) for IMP at CILE and NC-CILE in comparison with classic CPE and NC-CPE is caused by ionic conductivity of the binder which leads to a larger electroactive area. The use of accumulation period (240 s) results in peak current enhancements for both CILE and is larger for NC- CILE. This is because montmorillonite possesses a physical structure consisting of sheets of aluminosilicates [22]

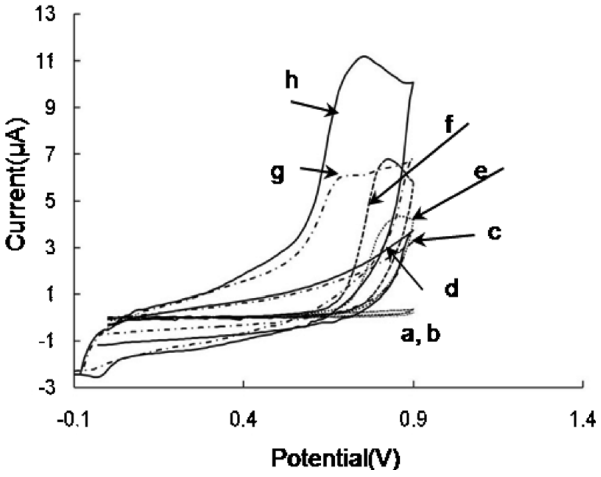

Fig.1. Cyclic voltammograms of (a) CPE, (b) NC-CPE, (c) CILE, (d) NC-CILE in the absence and (e) CPE, (f) NC- CPE, (g) CILE, (h) NC-CILE in the presence of 0.1 mM IMP in PBS 0.07 M (pH 7.2) at a scan rate of 50 mVs^{-1}.

which is neutralized by the intercalation of compensating, exchangeable Na^+. The Na^+ ion can be exchanged with a wide variety of hydrated inorganic or organic cations [23]. Several other researchers also applied the cation exchange property of montomorillonit for the adsorption of some cationic electroactive compounds on the surface of electrode [24,25]. Since IMP is protonated and has positive charge in the working solution (0.07 M PBS, pH 7.2), its interactions with montomorillonite nanoclays is similar to the other organic cationic species in this matrix. Therefore, NC-CILE was selected for further studies.

3.2. Effect of pH

The influence of the pH on the oxidation peak current of 0.1 mM IMP was investigated in the pH range of 2–7.2 applying the Britton–Robinson (B. R.) buffer (Fig. 2). At pH values higher than 8, the solubility of the drug is somewhat lowered due to the hydrophobic character of deprotonated molecule of IMP [4]. As seen, with solution pH raising the peak current increased and reached to the maximum value at pH 7.2. Since the pH 7.2 PBS gave the same response in terms of the peak current and the peak shape for IMP, PBS with pH 7.2 was used as the supporting electrolyte in all voltammetric determinations. In addition, the pH range of IMP, between 2 to 7.2 Ep, was a linear function of pH (Fig. 2. inset). From the plot of oxidation peak potential (Ep) versus pH, a slope of -0.029 V/pH was obtained, corresponding to the equation Ep (V) = 0.909 □ 0.029 pH. This result revealed that an unequal number of electrons and protons are involved in the oxidation of IMP. This is consistent with the previously proposed mechanism for the IMP oxidation [5, 26].

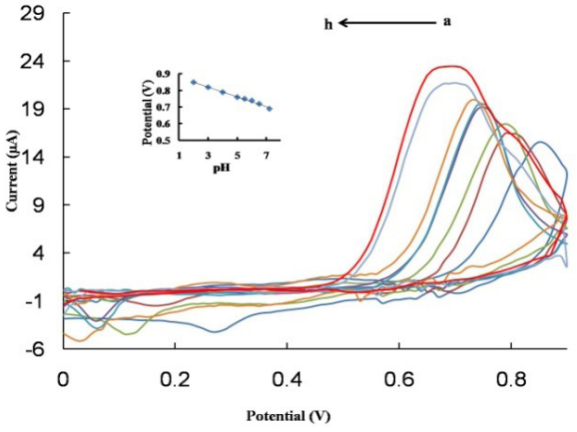

Fig. 2. Background subtracted cyclic voltammograms of 0.1 mM IMP at the NC-CILE; pH from a to h: 2,3,4,5,5.5,6,6.5,7.2 at 50 mVs^{-1}., accumulation time 240 s and accumulation potential 0 V. Inset: plot of oxidation peak potential vs. pH.

3.3. Effect of modifier

The effect of nanoclay as a modifier on the voltammetric response of the NC – CILE was optimized by varying its composition (2.5, 5, 10 and 15, % weight percent ratio). The results indicated that the peak currents increase with increasing nanoclay up to 10%, while further increase in the amount of nanoclay causes a decrease in the peak current. This is because the sites for desorption increase with the increase of nanoclay percentage in the modified electrode, while further nanoclay results in an increase in the resistance of the electrode, and consequently, it enhances the electron-transfer resistance. As a result, a NC – CILE (10%, w/w) was used in further studies.

3.4. Effect of accumulation potential and time

The accumulation potential as well as accumulation time is an effective factor which affects the response sensitivity. The effect of accumulation potential on the peak current of IMP was examined over the range of -300 to 500 mV keeping the accumulation time 240 s. The oxidation peak current increased up to 0 V. Therefore, an optimal accumulation potential of 0 V was used for further studies.

The accumulation time was changed from 0 to 300 s employing optimized accumulation potential value. It was observed that the peak current increased with accumulation time, in fact, the more IMP was adsorbed, the larger the peak currents became, and reached to a constant value after a certain accumulation period. Therefore, an accumulation time of 240 s was chosen for further experiments.

3.5. Study of the potential sweep rate effect

Cyclic voltammetry for 0.1 mM IMP was carried out at different scan rates (Fig.3). Results indicated that there is a linear relationship between the peak current (i_p) of IMP and the scan rate (v) in the range of 10 to 100 mVs^{-1} (Fig. 3, inset). With scan rate increasing, the anodic peak grew and the oxidation peak potential shifted to more positive potentials confirming the kinetic limitation in the electrochemical reaction [27].

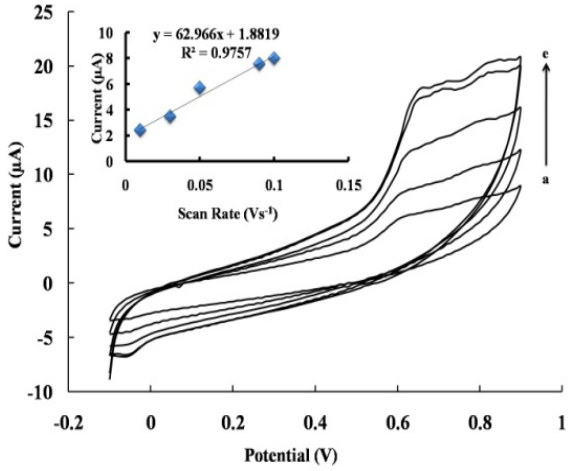

Fig. 3. Cyclic voltammograms of NC – CILE in 0.07M PBS (pH 7.20) containing 0.1 mM IMP at various scan rates: a-e (10 - 0 mVs^{-1}) . Inset: plot of peak current vs. scan rate.

Plot of log (peak current) vs. log (scan rate) for the surface-adsorbed IMP over 10–100 mV/s range, was linear. This plot had slope of 0.675 (correlation coefficient, 0.998) for IMP, respectively. The slope of 0.675 for log peak current vs. log scan rate implies that the redox process is located between those due to surface confined species and diffusive one. Wang et al. reported the slope of 0.64 for the plot of log peak current vs. log scan rate for IMP on a GCE [5] and attributed the deviation from theoretical value (the slope of 1 for log peak current vs. log scan rate) to the ECE mechanism of the redox process.

3.6. Calibration curve

The proposed method was employed for the determination of MP. In this respect, the relationship between the anodic peak current and the concentration of IMP was studied using cyclic voltammetry under the optimum conditions (Fig.4). The analytical curve shown (Fig.4.inset) has linear calibration range of concentration over the range of 0.1–2 μM with the regression equation of Ip (μA) = 2.859 + 1.714C (μM), and over the range of 2- 40 μM

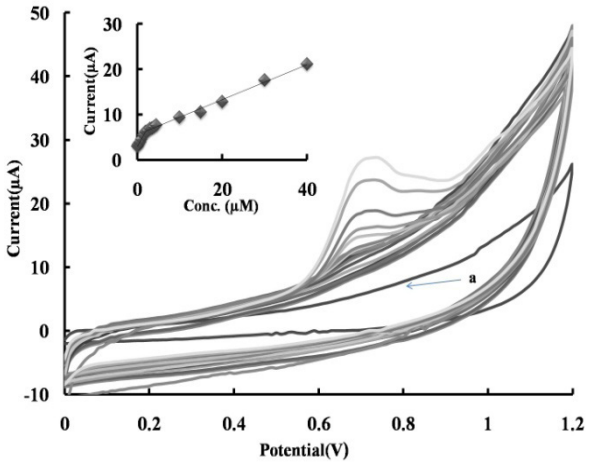

Fig. 4. Cyclic voltammograms of NC- CILE in 0.07 M PBS, pH 7.2 in the presence and (a) in the absence of different concentrations of IMP measured, accumulation time 240s and accumulation potential 0 V. Inset shows the calibration curve of peak current vs. IMP concentration.

with the regression equation of Ip (μA) = 0.386 + 5.546C (μM), and with correlation Also, the limit of detection (signal-to-noise ratio of 3) was 19 nM. The electrochemical responses

Table1. Electrochemical detection of IMP reported at various electrodes

Modified electrodes	Linear range (μM)	Detection limit (nM)	Reference
AuNPs-ITO	1000 5-	1	[3]
GPCE (graphite polyurethane composite electrode)	0.3–3	4.6	[1]
BDE	0.05 –100	3	[2]
ß-CD-CPE (carbon paste electrode modified with β-cyclodextrin)	0.1–1	20	[4]
PNI-CPE (poly(N-vinylimidazole) modified CPE)	60-800	-	[6]
NC –CILE	0.1-2 2-40	19	This work

of the NC-CILE in terms of linear range and detection limits were compared to the other modified electrodes, which were reported in the literature (Table.1). The performance of the electrode for IMP determination was also comparable to previously reported works. The easy preparation of the proposed electrode with low cost should also be considered.

3.7. Stability, repeatability and reproducibility of the electrode

Stability of The NC – CILE was checked by recording the response of the electrode in 2 μM of IMP after every few days. The NC-CILE shows high stability for IMP detection and retains 90.1% of its original response to IMP after 30 days of storage. In order to study the repeatability of the electrode preparation procedure, 7 modified electrodes based on the same fabrication procedure were prepared and used for the determination of 2 μM of IMP. The relative standards deviation (RSDs) of 2.73% revealed good repeatability. The responses of four similar electrodes were separately measured toward 2 μM of IMP, and RSDs of 2.97% was obtained confirming high reproducibility of the fabrication method. The response of the proposed composite electrode was evaluated toward some common species found in biological fluids such as glucose, ascorbic acid, uric acid. The tolerance limit was defined as the maximum concentration ratio of interfere/ IMP causing an error less than ±5.0% for the determination of IMP.
In the presence of 10 μM IMP the results showed that 100-fold excess of glucose; 100- fold excess of ascorbic acid and 50-fold excess of uric acid; did not interfere with the analysis of IMP. The results demonstrated good selectivity for the proposed electrode.

3.8. Real sample analysis

In this work, we applied nanocomposite electrode in order to determine IMP in urine sample. Standard addition method was used for measuring IMP concentration in the sample. Urine sample was also diluted with 0.07 M PBS (pH 7.2) and then appropriate amount of this diluted sample was transferred to the electrochemical cell for the determination of IMP, as reported in Table 2. The results confirm that the NC –CILE retained its efficiency for the determination of IMP in urine sample.

Table 2: Determination of IMP in urine sample using the proposed method (n=3)

Sample	Added (μM)	Found (μM)	Recovery (%)
urine	0	N.D.*	-
	0.5	0.52(±0.02)	104.0
	1.0	0.97(±0.04)	97.0
	1.5	1.52(±0.03)	101.3

• Not detected

4. Conclusion

This work was aimed at the determination of IMP in urine sample. For this purpose, NC –CILE was fabricated and further used for sensitive determination of IMP. An effective accumulation of the drug molecules has been found on the electrode due to synergistic effect of nanoclays and IL. High stability and reproducibility as well as the ease of preparation, low cost and surface renewal made us to use this electrode in our study.

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