Asian Journal of Chemistry; Vol. 24, No. 4 (2012), 1747-1750

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

Development of Polymer Composite Electrode to Analyze Metformin Hydrochloride Drug in Pharmaceutical Formulation with Higher Current Response

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(*Received*: 22 April 2011; *Accepted*: 25 November 2011) AJC-10754

A composite polymer of polyaniline (PANI) and polypyrrole (PPy) was coated on a tin oxide slide, offers improvement in voltammetric detection system compared to conventional platinum electrode. Polyaniline/polypyrrole composite electrode was developed by electrochemical deposition technique and standardize as a working electrode in cyclic voltammetric technique for the detection of metformin hydrochloride (MET) drug. Metformin hydrochloride is a drug used for diabetics patients gave one well defined reduction peak (c_1 at 220 mV) and one oxidation peak (a_1 at 1266 mV) at composite polymer electrode. The results are compared with that of a platinum electrode (c_1 at 740 mV and a_1 at 1308 mV, respectively). It was observed that the peak current increases significantly at pH = 3 on the composite polymer electrode and both reduction and oxidation peak potentials shift to lower potential than that of potential observed at platinum electrode. It indicates catalytic behaviour of composite polymer electrode for the analysis of metformin hydrochloride. A cyclic voltammetric method for determination of metformin hydrochloride at composite polymer electrode is proposed in this paper. The best results for the oxidation of metformin hydrochloride at pH = 3 with composite polymer electrode were obtained at a potential of 1266 mV in presence of Ag/AgCl reference electrode.

Key Words: Composite polymer, Electrochemistry, Metformin hydrochloride.

INTRODUCTION

The activity in new electrode materials has been growing over the last 20 years and is motivated by the need to develop well-defined surfaces for studying electron exchange processes for controlling electrochemical reactions. Among the materials useful for electrode preparation, conducting polymers are potentially attractive materials[1] due to their moderately high conductivity, low cost, relatively high stability and facile production by electrodeposition[2]. The formation of composites of these conducting polymer, is one of the most useful tools in polymer science in which the physical and mechanical properties of a polymer can be controlled and enhanced[3]. Polyaniline and polypyrrole films show good electrical conductivity and are relatively stable over long period of time under ambient conditions. The mechanical and electrical properties of these polymers can be enhanced by appropriate choice of anion, electrode material or by composite formation. Improved mechanical properties were observed in composites and doped conjugated polymer due to the increase in molecular weight[3-6]. The polyaniline/polypyrrole composites[7] had conductivity in the range of 10^{-2} to 10^{-3} S/cm depending on experimental conditions. Karakisla and Sack[8] prepared the free standing polymer film of polyaniline and polypyrrole on insulating polycarbonate electrode. Polyaniline/polypyrrole film composite with high electrical conductivity and good mechanical properties were reported by Yang *et al.*[9].

The composite films were flexible and strong enough and have electrical conductivity as high as 5-6 S/cm. Polyaniline-polypyrrole composite coating were electrochemically synthesized by Rajagopalan *et al.*[10] on low carbon steel for corrosion protection. In our previous papers[11,12] the FTIR and UV-VIS and SEM studies showed the existence of certain interaction take place between polyaniline and polypyrrole. This fact was supported by thermogravimetric analysis which showed that the composite possesses higher stability than either polyaniline or polypyrrole films separately. The unusual dual band gap character and I-V characteristics of polyaniline/polypyrrole composite gave intermediate results corresponding to polyaniline and polypyrrole films, which indicate that composite film was conducting with better thermal stability.

However, the areas of the applicability of conducting polymers are very rich[13-19]. Many papers on the study of drug delivery system on modified electrode are also available[19-21].

Present paper reports the preparation and systematic study on cyclic voltammetric investigation of metformin hydrochloride in pharmaceutical formulation.

Metformin hydrochloride (MET, Fig. 1) is an antidiabetic drug from the biguandide class of oral hypoglycemic action and is one of most commonly prescribed medicines for type II diabetes, participates in biological and pharmacological processes[20,21]. Metformin hydrochloride is the only antidiabetic drug that has been proven to reduce the cardiovascular complications of diabetes, as shown in a large study of overweight patients with diabetes[22]. Several methods have been developed for determination of metformin hydrochloride, including liquid chromatography-tandem mass spectrometry[23-25], capillary electrophoresis[26], high-performance liquid chromatography[27-29] and ion-pair high-performance liquid chromatography[30,31]. Electroanalytical methods are highly sensitive, simple in operation and require low-cost apparatus. Electroanalytical methods for the determination of metformin hydrochloride was proposed by Tian *et al.*[32] at a combination of molecular wire and carbon nanotubes and in the presence of Cu(II) ions[33]. But the current observed on these electrodes was low and the behaviour of the drug was entirely different as observed at polyaniline/polypyrrole composite polymer electrode in methanol as a solvent.

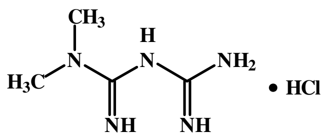

Fig. 1. Molecular structure of metformin hydrochloride ($C_4H_{11}N_5$·HCl)

EXPERIMENTAL

Polyaniline films were deposited on tin oxide coated glass slide using cyclic voltammetric technique (using Eg & G Princeton applied research model 273; the potentiostat was controlled by the electrochemistry software 4.30 A). For electrochemical deposition of polymer tin oxide coated glass slide was used as working electrode, Ag/AgCl reference electrode and graphite rod as counter electrode. Sulphuric acid (10^{-1} M) and sodium perchlorate (Aldrich) (10^{-2} M) were used as doping agents for polyaniline formation. Aniline (99.8 %) was procured from Aldrich chemicals and redistilled before use. The voltage applied was varied from (-0.3) V to (+1.0) V and the concentration of aniline was taken 0.2 M. On this pre-existing polyaniline film, polypyrrole film was deposited electrochemically by constant potential coulometry at constant potential 0.8 V. The deposition was allowed till the accumulated charge reaches 15 coulombs. The concentration of pyrrole (99 % Aldrich) was 0.2 M and the amount of supporting electrolyte *p*-toluene sulphonate was taken 0.1 M. All the films were prepared in aqueous media and stored in air at room temperature.

General procedure

Activation of electrode: The prepared polyaniline/polypyrrole composite polymer coated on tin oxide coated glass slide was then activated as a working electrode in cyclic voltammetric investigations. To obtain a more sensitive and stable voltammetric response the working electrodes were cyclically scanned 20 times in the potential range from (-1.6) V to (+1.2) V to get a stable background current.

Preparation and analysis of drug sample: Ten tablets of metformin hydrochloride (Glycomet USB pharmaceutical, India), each containing 500 mg of metformin were powdered in a mortar and the amounts corresponding to 1 × 10^{-3} M of metformin hydrochloride were weighted and dissolved in methanol. The content of the flask were sonicated for 15 min to affect complete dissolution. After the excipients have settled down, an aliquot of the clear supernatant was transferred quantitatively into a calibrated flask and diluted to a final volume of 10 mL with methanol. Determination of metformin hydrochloride in working solution was performed by the cyclic voltammetric procedure.

For the analysis of metformin hydrochloride on platinum electrode, platinum was used as working electrode, Ag/AgCl as reference electrode and Pt rod as auxiliary electrode. When analysis was carried out at composite polymer electrode, activated polyaniline/polypyrrole composite polymer electrode was used as working electrode in place of platinum electrode.

Detection method: In order to understand the electrochemical activity of polyaniline/polypyrrole composite polymer electrode, the cyclic voltammetry of metformin hydrochloride drug in pharmaceutical formulation was carried out. Metformin hydrochloride was studied systematically in the pH range 1.8 to 12 in Britton-Robinson (BR) buffers. At pH 3 and 6 metformin hydrochloride was found to give two peaks one reduction peak (c_1) and one oxidation peak (a_1) (Fig. 2a) and these peaks are attributed to the reduction and oxidation of =NH and $-NH_2$ groups respectively as shown in Fig. 2b.

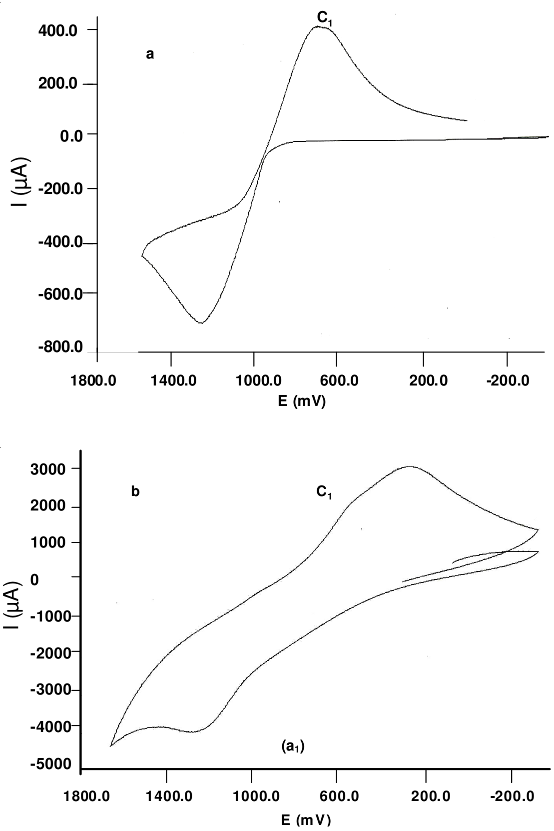

Fig. 2. Metformin hydrochloride on composite polymer film (a) pH = 6 (b) pH = 3

The effect of different scan rate on the electrode process was studied by recording cyclic voltammograms at various sweep rates from 10-300 mV/S in 1 mM solution of metformin hydrochloride. No evidence of reversibility was observed for the peak in the range 10-300 mV/S. The peak current i_p (μA) was found to increase proportionally with square root of scan rate $\nu^{1/2}$ (mV/S) (Fig. 3). The correlation equation was i_{pa}/mA = 504.95 + 333.29$\nu^{1/2}$ (mV/S) (r - 0.997), which confirmed the diffusion controlled behaviour of the electrode process. The cyclic voltammograms were also recorded in the concentration range 1 to 0.01 mM for metformin hydrochloride. The peak current for metformin hydrochloride at 20 mV/S increases linearly from 0.01 to10 mM concentrations (Table-1) and correlation equation was 6.16 + 769.51C (mM) (r = 998).

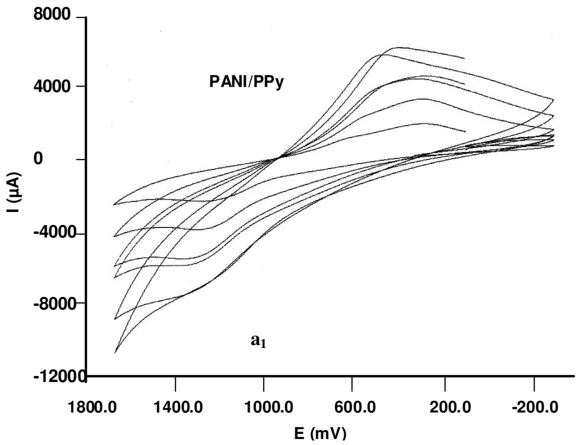

Fig. 3. Effect of different scan rates on the cyclic voltammetric behaviour of metformin hydrochloride on composite polymer thin film at 1 mM concentration and at pH 3

TABLE-1
EFFECT OF DIFFERENT CONCENTRATION ON OXIDATION (i_{pa}) PEAK OF METFORMIN HYDROCHLORIDE AT POLYANILINE/POLYPYRROLE COMPOSITE POLYMER ELECTRODE AT pH 3

S. no.	Concentration (mM)	Current (μA)
1	0.10	190.00
2	0.25	210.00
3	0.50	227.00
4	1.50	1111.2
5	3.40	2767.65
6	4.00	3120.0
7	6.00	4545.2

RESULTS AND DISCUSSION

We have compared the results obtained at polyaniline/polypyrrole electrode for metformin hydrochloride with platinum as a working electrode. Good results were observed at composite polymer electrode as compared to Pt electrode. Platinum electrode shows poor current response (i_{pc} = 423 mA) and substantially higher potential (E_{pc} = 740 mV), specially at pH 3. Whereas polyaniline/polypyrrole composite polymer electrode shows reduction peaks with better current response (i_{pc} = 4.06 mA) and lower potential (E_{pc} = 220 mV). This indicates catalytic behaviour of composite polymer film with relatively high sensitivity and stability as shown in Fig. 4.

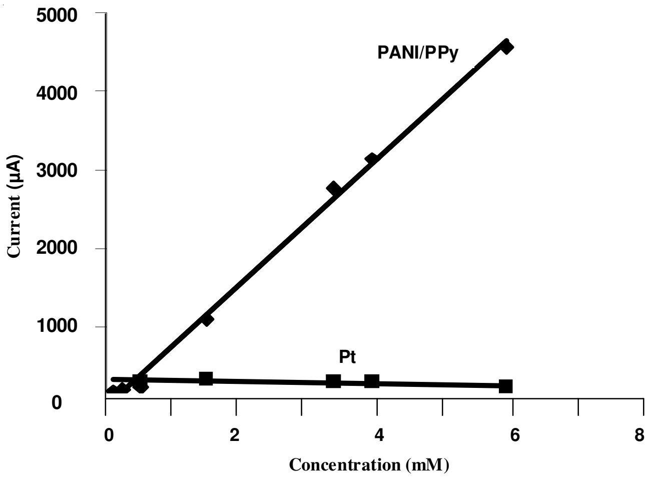

Fig. 4. Comparison of electrochemical response of metformin hydrochloride at composite polymer film with that of the conventional platinum electrode.

This composite polymer electrode showed unusual pH dependent behaviour. The current at pH 3 increases significantly with catalytic shift in potential at lower potential range comparative to that of other pH values of the solution. Fig. 5 and Table-2 show a comparative pH dependent behaviour of metformin hydrochloride at composite polymer electrode with that of platinum electrode.

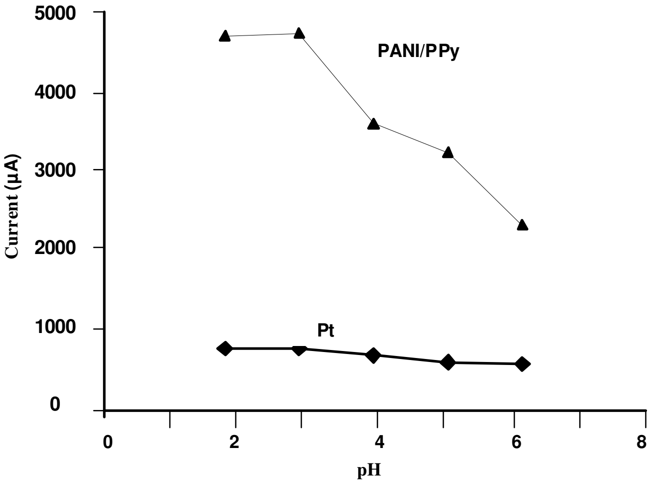

Fig. 5. Comparative pH dependent behaviour of metformin hydrochloride at composite polymer electrode with that of the conventional Pt electrode at 6 mM concentration

TABLE-2
A COMPARATIVE pH DEPENDENT BEHAVIOUR OF METFORMIN HYDROCHLORIDE AT COMPOSITE POLYMER ELECTRODE WITH THAT OF PLATINUM ELECTRODE AT 6mM CONCENTRATION

pH	Composite polymer electrode current (i_{pa}) μA	Current (μA)
2	4510.0	756
3	4545.2	760
4	3452.0	672
5	3102.0	607
6	2231.0	580

Analytical Application of polyaniline/polypyrrole polymer film for the determination of metformin hydrochloride:

The electrochemical behaviour of metformin hydrochloride on polyaniline/polypyrrole modified electrode was established and studied for the first time. Metformin hydrochloride is irreversibly reduced and oxidized at this electrode. It showed that the metformin hydrochloride concentration in pharmaceutical formulations can be determined by using voltammetric technique on the basis of their oxidation process. This behaviour provided a useful tool for the detection and quantification of drugs at low levels of drug concentration. The procedure showed a clear advantage such as no pretreatment or time-consuming extraction steps could be avoided for pharmacokinetic studies as well as for quality control laboratory studies.

Conclusion

Polyaniline/polypyrrole composite polymer film electrode was successfully prepared by electrochemical polymerization on tin oxide coated glass slide. This polyaniline/polypyrrole composite polymer film showed good electrochemical response towards the metformin hydrochloride drug as compared to the platinum electrode. This electrode also showed good adherence to the substrate and provides a sensitive and selective method of metformin hydrochloride analysis. The improvement in metformin hydrochloride detection indicates good promise for qualitative and quantitative analysis.

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