Nanostructured polyaniline modified electrode for the quantification of the Paracetamol in the pharmaceutical samples

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ABSTRACT

Adsorptive stripping voltammetric procedure for determination of the paracetamol on the nanostructured polyaniline film modified glassy carbon electrode in the pharmaceutical formulations was described. The effect of pH was studied in different mediums such as pH 1.0 to pH 13.0. The voltammetric detection of paracetamol was carried out from −0.5 V to 1.2 V _versus_ Ag/AgCl using the nanostructured polyaniline modified glassy carbon electrodes. The electroanalytical parameters of the sensor were highly dependent on their configuration and on the dimensions of the carbon electrode. From the study of scan rate variation, the electrode process was found to be diffusion controlled. The concentration effect of the paracetamol was studied. The best limit of detection obtained for the paracetamol was 100 ppb and the linear range from 200 to 600 ppb at the modified electrode surface. The sensor were successfully applied for the detection of paracetamol in the several pharmaceutical drug formulations. The Atomic Force Microscopic (AFM) image shows the surface morphologies of polymer modified electrode, compound adsorbed surface, particle distribution graphs and surface roughness values which are in good agreement.

Keywords: Paracetamol, Voltammetry, Nanostructure, Polyaniline, differential pulse Voltammetry, AFM.

1. INTRODUCTION

Non-steroidal anti-inflammatory drugs of paracetamol, N-acetyl-p-aminophenol or acetaminophen is one of the most commonly used drugs in the world. It is the preferred alternative analgesic and antipyretic to aspirin, particularly for the patients who cannot tolerate aspirin [1, 2]. Paracetamol rapidly gets absorbed and distributed after the oral administration and is easily excreted in urine [3]. Generally it is highly effective for the release of pain associated with artralgia, neuralgia and headache and even to the patients of gastric symptoms. In most of the countries it is used as a substitute for aspirin [4]. Paracetamol is easily and completely metabolized, normally it does not show any harmful side-effects. However, the over dosage causes the accumulation of toxic metabolites leading to kidney damage, liver disorders, skin rashes, inflammation in the pancreas and may lead to death [5]. Therefore, it is very important to establish a simple, fast, sensitive and accurate detection method for the paracetamol.

Conducting polymer can be synthesized by both the chemical and electrochemical procedures. Both methods for obtaining high quality polymers are widely used. Through the electrochemical method, a polymer can be synthesized by applying the potentiostatic or galvanostatic conditions or by using the cyclic voltammetryv [6-13]. Advantage of the electrochemical synthesis is the ability to control the polymerization process (for example, the polymerization rate or the thickness of the resulting polymer) by changing the current, potential, the scanning rate potential or the

number of voltammetric cycles [6-13]. Chemical synthesis is suitable when the bulk quantities of the polymer are necessary and up to date it presents the dominant commercial method of producing the electronically conducting polymers. The polymers (Thus-delete) obtained through the chemical synthetic route are in an oxidized, high conductivity state containing the counterions incorporated from the solution used in the preparation procedure.

In recent decades, conducting polymer nanostructures have received an increasing attention in both the fundamental research and various application fields including sensors owing to its unique properties at the nanoscale. A promising way of controlling the polymer bulk properties, such as conductivity, processability, thermal and mechanical stabilities is through the organization of the polymeric chains in the nanometer scale. Nanostructural morphology of conducting polymers could be prepared by the template-free or surfactant-free chemical method (self-template method). In this synthesis route, the monomer of conducting polymers or its salts form the micelles by themselves, which act as templates for the formation of nanostructures.

Electroanalytical methods are simple, economical, rapid and sensitive to reach the lower limit of detection. Among the electro-analytical techniques, voltammetry coupled with the pulse waveform is considered as a highly sensitive technique with the very low detection profiles attributed to zero background current. The differential pulse voltammetric behaviour of some drugs including the acetaminophen at various conducting polymers electrode is reported [14-21]. Electrochemical detection and cyclic voltammetric determination of acetaminophen are reported [22-27].

This work is aimed at developing a simple and sensitive electro-analytical method for the determination of paracetamol on the nanostructured polymer modified electrodes.

2.0 Material and Methods

2.1 Apparatus and Reagents

All the voltammetric measurements were carried out using a single-compartment three electrode cell setup with the nanostructured polyaniline modified glassy carbon electrode as the working electrode, Ag/AgCl as the reference electrode and platinum wire as an auxiliary electrode. Differential Pulse Voltammetry (DPV) and Cyclic Voltammetry (CV) experiments were carried out using an CH Instruments Electrochemical Workstation (model CH 650C). All

potentials given are with respect to the potential of the reference electrode. The pH measurements were performed with a Hanna instrument pH/ORP meter using a combination glass electrode. A 200 ppm stock solution was made up in aqueous ethanol. To study the aqueous media, Britton Robinson Buffers, 0.1 mol.dm^{-3} KOH, KCl and 0.1 mol dm^{-3} H$_2$SO$_4$ in 50% aqueous alcohol were used as the medium for the analysis. paracetamol was purchased from the Merck AR grade. Surface analysis done by the Nanosurf Easy scan 2 AFM under the following conditions: scan direction – up, Time/Line – 206 ms, Tip voltage - 1.0 V, Vibration frequency – 169.969 KHz, Measurement environment – air and Operating mode – Dynamic force.

2.2. Modification of the Electrodes

A GCE (3-mm diameter) was polished using 1.0 and 0.05 mm alumina slurry and rinsed thoroughly with the Milli- Q water. Ultrasonic agitation for 30 min of 2.0 mg of chemically prepared nanostructured polyaniline in 2 mL of water gave a homogeneous green solution. 20 μL of this solution was placed on the GCE surface. After that the electrode was then dried at the room temperature to obtain a polymer modified GCE.

2.3 Pharmaceutical sample preparation

One tablet which contains paracetamol were weighed, powdered and then placed into a 250 ml of conical flask; warm water was added into the flask. The sample was swirled to dissolve for 30 minutes in sonicator and left to cool. The sample solution was filtered through a filter paper (Whatman No.42) into 100 ml volumetric flask.

3.0 Results and discussions

3.1 Characterization of electrode surfaces

Figure I displays the AFM image of the nanostructured polyaniline and the paracetamol adsorbed on GCE. The polymer film is uniformly coated on the electrode surface and formed a nanorod -like porous reticulated morphology. The compound adsorbed surface exhibits a granular adsorbed nanosize rod like photographs. This surface morphology is used to find the active surface area of the composite electrode is 5 times greater than the geometric area. The figure shows the surface morphologies of polymer modified electrode, compound adsorbed surface, particle distribution graphs and surface roughness values.

3.2 Effect of pH

The effect of buffer pH on the electrochemical response of the nanostructured polyaniline/GCE towards the paracetamol is investigated using CV. Variations of the peak current with respect to pH
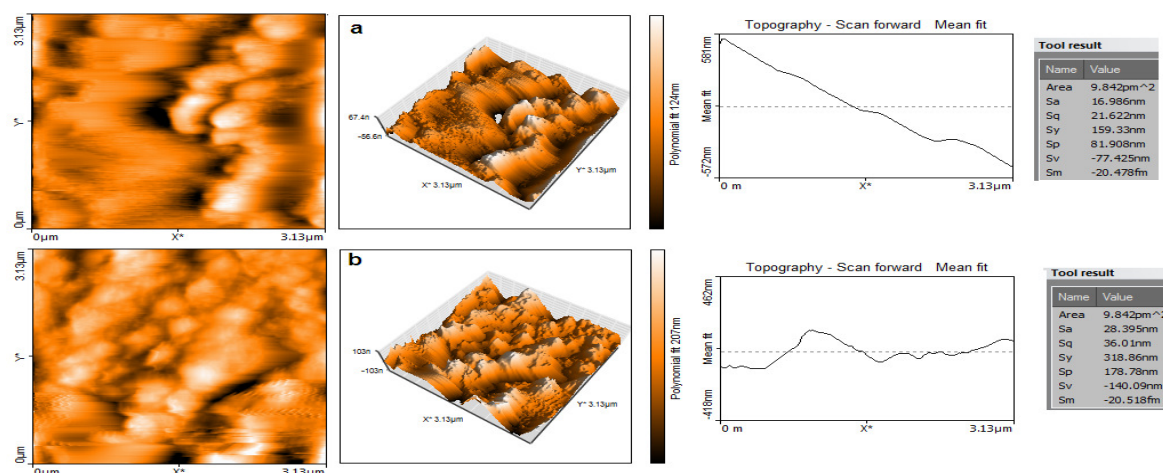
Figure - 1: AFM photographs of (a) Nanostructured polyaniline (b) Compound adsorbed polymer modified electrode surface of 2D, 3D, Particles distribution graphs and roughness data.

Table – 1: Optimum experimental conditions in DPSV		
Variable	**Range studied**	**Optimum value**
pH	1-13	1.0
Accumulation potential (V)	0.1 to 0.5	0.5
Accumulation time (Sec)	10-60	10
Initial scan potential (V)	-0.5 to 0.3	0.1
Pulse Height (PH) (mV)	25 to 150	50
Pulse width (PW) mSec	25 to 150	50
Scan Increment (SI) mV	2 to 20	4
Scan rate (SR) mV/sec	10 to 100	50
Stirring rate (rpm)	50 to 250	250
Rest period (Sec)	2 to 10	5

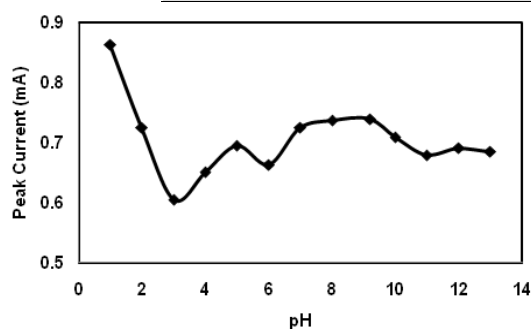| Table – 2: The amount of compounds are determined by DPSV in tablets			
Brand name	**Company name**	**Tablets**	**Experimental value**
Crocin	Glaxosmithkline	500 mg	488 mg
Calpol	Glaxosmithkline	500 mg	495 mg
Cyclopam	Indoco	500 mg	488 mg
Doliprane	Nicholas piramal	500 mg	499 mg
Colimex tabs	Wallace	500 mg	493 mg

Figure - 2: Curve of peak current *vs* pH.

of the electrolyte in the pH range from 1.0 to 13.0 are shown in the Figure 2. The anodic peak currents of the paracetamol increase with the solution pH 1.0. However, in the higher pH the paracetamol oxidation peak current starts to decrease. A pH value of 1.0 is chosen as an optimum pH for the further experiments.

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3.3. Cyclic voltammetry behavior of the paracetamol

Cyclic voltammograms of the paracetamol are recorded using the nanostructured polyaniline modified glassy carbon electrode in the acid, at 100 mV/sec scan rate. Figure III represents the cyclic voltammogram of 300 ppm paracetamol at pH 1.0. The cyclic voltammogram exhibited one oxidation peak and one reduction peak with the small current responds. Peak current dependence on the scan rate is studied by varying the scan rate from 25 to 500 mv/sec at a concentration 300 ppm.
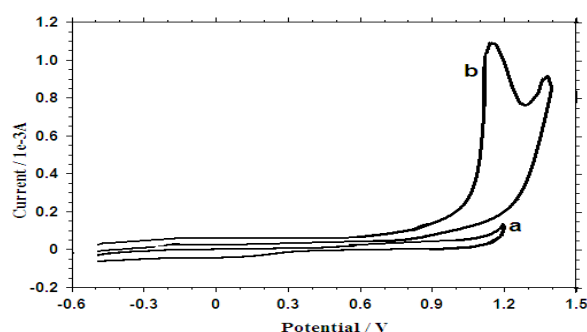

Figure – 3: Cyclic voltammogram of (a) nanostructured polyaniline modified electrode surface, (b) 300 ppm paracetamol on nanostructured polyaniline modified electrode at 100 mV/s in pH 1.0.

Peak current against the scan rate results in curved lines while peak current vs. square root of the scan rate lead to the straight lines with a good correlation (ip = 8.325$\square$ + 54.664, r^2 = 0.997). This suggests the diffusion controlled electron transfer in both the cases. Log values of peak currents are plotted with the log scan rates and the straight lines are obtained as ip = 0.309$\square$ + 1.6454, r^2 = 0.997. The fractional slope values confirm the diffusion controlled oxidation process.

3.4 Differential pulse stripping analysis of the Paracetamol

Cyclic voltammetric results revealed the electroactive nature of the paracetamol in the nanostructured polyaniline modified glassy carbon electrode at pH 1.0. Hence the differential pulse stripping voltammetric study is carried out. Experiments are carriedout to find out the best accumulation potential in the chosen pH 1.0 in the solution containing 200 ppb for the stripping analysis.

The accumulation potentials (E_{acc}) are varied from 100 to 500 mV for AAP at deposition time (DT) of 10 seconds. It shows the maximum peak current for an accumulation potential in the 500mv. Deposition time is varied from 10 to 60 s.

The maximum current response is observed at 10 s. The Initial scan Potential (IP) is also an important parameter like accumulation potential. The initial scan potential is varied between -0.5 and 0.3V the stripping peak current is measured maximum at 0.1 V.

The factors affecting the striping step i.e. primary oxidation process which are responsible for the determination, were varied and optimized. The influences of the pulse height, pulse width potential scan increment and the scan rate are studied in various values and the maximum peak current conditions are found out. The range of study and optimized conditions are presented in the table 1. The optimum conditions which resulted in maximum peak current response are used to study the effect in analyte concentration.
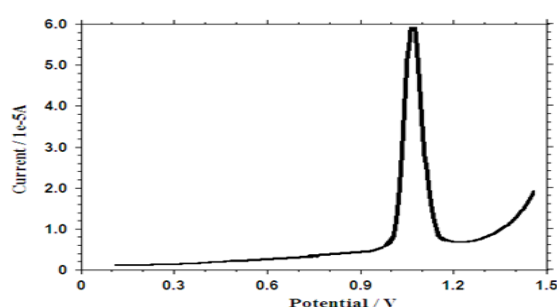

Figure – 4: Differential pulse stripping voltammetric behavior of paracetamol on nanostructured polyaniline modified GCE under optimum conditions.
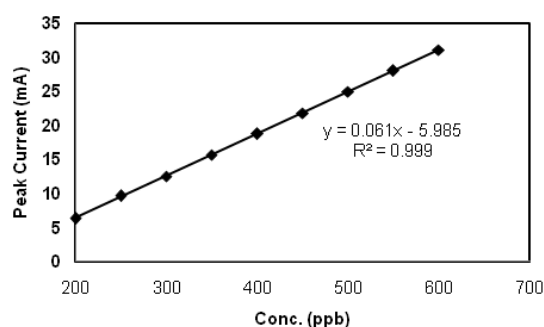

Figure – 5: Calibration plot of current *vs.* concentration of paracetamol.

3.5 Analytical characteristics

The experimental results shows that the peak current increased with the increase of paracetamol concentration. A representative differential pulse stripping voltammogram is given in the figure IV. A calibration plot was made and shown in the figure V, which indicats the linear dependence of the peak current with the concentration under the optimum experimental condition that led to the maximum peak current. The Limit Of Detection (LOD) is found as 100 ppb. The reproducibility of the stripping signal is

realized in the terms of relative standard deviation for 10 identical measurements carried out at a concentration level of 200 ppb.

3.6 Proposed method for the determination of drug in pharmaceutical

The pharmaceutical samples which contains Paracetamol were collected from the medical shops. The tablets were powdered, dissolved and subsequently diluted to a required concentration. Differential pulse stripping voltammograms of the Paracetamol at pH 1.0 were recorded under the optimum experimental conditions. By substituting the peak current in the calibration plot and keeping the dilution factor in consideration, the amount of paracetamol in the tablet was determined and the results are presented in the table 2.

4.0 Conclusion

The polymer nanostructures were used to modify the GCE for the electrochemical detection of Paracetamol. Due to the electrode's simple fabrication procedure, wide linear range, low detection limit for detection was achieved. The effects of potential interferents were studied and were found to be insignificant. When the procedure was used for the determination of samples, satisfactory results were obtained without the necessity of time-consuming the sample pretreatments or data analysis. The simple fabrication procedure, high analysis speed, reproducibility, structural stability, wide linear dynamic range and high sensitivity, suggest that the proposed sensor is an attractive candidate for the practical applications.

5. REFERENCES

1. Babaei A, Garrett DJ, Downard AJ. Selective Simultaneous Determination of Paracetamol and Uric Acid Using a Glassy Carbon Electrode Modified with Multiwalled Carbon Nanotube/Chitosan Composite. **Electroanalysis**. 2011; 23: 417 -423.

2. Kuskur CM et al., Electrochemical Investigation of Paracetamol at Poly(Glycine) Modified Carbon Paste Electrode: A Voltametric Study. **Journal of Analytical Bioanalytical Techniques.** 2015; 6: 1-6.

3. Babaei A; Taheri AR, Afrasiabi M. A Multi-Walled Carbon Nanotube-Modified Glassy Carbon Electrode as a New Sensor for the Sensitive Simultaneous Determination of Paracetamol and Tramadol in Pharmaceutical Preparations and Biological Fluids. **Journal of Brazilian Chemical Society.** 2011; 22: 1549-1558.

4. Qouatli SE. Electrochemical Studies and Square Wave Voltammetry of Paracetamol at Managanese Modified Carbon Paste Electrode. **Pharmaceutical Analytica Acta**. 2013; 4: 1-5.

5. Goyal RN, Singh SP. Voltammetric determination of paracetamol at C_{60}-modified glassy carbon electrode. **Electrochimica Acta**. 2006; 51: 3008-3012.

6. Manisankar P et al., Influence of surfactants on the electrochromic behavior of poly (3,4-ethylenedioxythiophene). **Journal of Applied Polymer Science.** 2007: 104; 3285–3291.

7. Manisankar P, Vedhi C, Selvanathan G. Synthesis of a nanosize copolymer of 3,4-ethylenedioxythiophene with diclofenac and characterization. **Journal of Polymer Science Part A: Polymer Chemistry**. 2007; 45; 2787-2796.

8. Manisankar P et al., Copolymerization of aniline and 4,4′-diaminodiphenyl sulphone and characterization of formed nano size copolymer. **Electrochimica Acta**. 2006; 52: 831-838.

9. Manisankar P et al., Electrochemical synthesis and characterization of novel electrochromic poly (3,4-ethylenedioxythiophene-co-Diclofenac) with surfactants. **Electrochimica Acta**. 2006; 51: 2964-2970.

10. Manisankar et al., Electrochemical and electrochromic behavior of novel poly (aniline-co-4, 4'-diaminodiphenyl sulfone). **Chemistry of Materials**. 2005; 17: 1722-1727.

11. Manisankar P, Vedhi C, Selvanathan G. Synthesis and characterization of novel nano size electroactive poly 4, 4′-diaminodiphenyl sulphone. **Journal of Polymer Science Part A: Polymer Chemistry**. 2005; 43: 1702-1707.

12. Yu D. Oriented Assembly of Fe3O4 Nanoparticles into Monodisperse Hollow Single-Crystal Microspheres. **Journal of Physical Chemistry B.** 2006; 110: 21667-21671.

13. Arruebo M et al., Development of Magnetic Nanostructured Silica-Based Materials as Potential Vectors for Drug-Delivery Applications. **Chemistry of Materials**. 2006; 18: 1911-1919.

14. Vadivel M. **Journal of Chemical and Pharmaceutical Sciences**. 2015; 7: 200-202.

15. Raja JDl, Synthesis, structural characterization, electrochemical, biological, antioxidant and nuclease activities of 3-morpholinopropyl amine mixed ligand

complexes. **Journal of Chemical and Pharmaceutical Research.** 2015; 7: 1-14.

16. Fernando J, Vedhi C. Synthesis, Spectral and Electrochemical Characterization of Adipic Acid Doped Polyaniline. **The International Journal of Science & Technology.** 2015; 3: 166-173.

17. Lakshmi A et al., Electroanalysis of Diazepam on Nanosize Conducting Poly (3-Methylthiophene) Modified Glassy Carbon Electrode. **Journal of New Materials for Electrochemical Systems**. 2014; 17: 185-190.

18. Lakshmi A, Vedhi C. Synthesis and Characterization of Poly (3-hexylthiophene) and Used as Modified Electrode for Determination of Antidepressants in Pharmaceutical Formulations and Urine Samples Physical and Analytical Electrochemistry, Electrocatalysis, and Photoelectrochemistry. **Journal of The Electrochemical Society**. 2013; 160: H252-H257.

19. Lakshmi A. **Electrochimica Acta**. Electrochemical, electrochromic behaviour and effects of supporting electrolyte on nano-thin film of poly (3, 4-ethylenedioxy thiophene). 2013; 92: 452-459.

20. Sikkander MA, Vedhi C, Manisankar P. Cyclic Voltammetric determination of 1, 4-Dihydro pyridine drugs using MWCNTs modified glassy carbon electrode. **Der Chemica Sinica**. 2012; 3: 413-420.

21. Sikkander MA, Vedhi C, Manisankar P. Electrochemical stripping studies of amlodipine using Mwcnt modified glassy carbon electrode. **Chemistry and Materials Research**. 2011; 1:1-7.

22. Gopu G et al., Determination of three analgesics in pharmaceutical and urine sample on nano poly (3, 4-ethylenedioxythiophene) modified electrode. **Ionics.** 2012; 18; 231-239.

23. Gopu G et al., Stripping voltammetric determination of analgesics in their pharmaceuticals using nano-riboflavin-modified glassy carbon electrode. **International Journal of Electrochemistry**. 2011; 2011: 1-11.

24. Vedhi C et al., Synthesis of potential capacitive Poly 4, 4′-diaminodiphenyl sulphone–metal nanocomposites and their characterizations. **Synthetic Metals**. 2010; 160; 1307–1312.

25. Raj JA et al., Electrochemical synthesis of nanosize polyaniline from aqueous surfactant solutions. **Materials Letters**. 2010; 64: 895-897.

26. Muralidharan B et al., Determination of analgesics in pharmaceutical formulations and urine samples using nano polypyrrole modified glassy carbon electrode. **Journal of Applied Electrochemistry.** 2009; 39: 1117-1184.

27. Muralidharan. oltammetric determination of analgesics using a montmorillonite modified electrode. **Applied Clay Science**. 2008; 42: 206–213.