Anal. Bioanal. Electrochem., Vol. 10, No. 11, 2018, 1437-1448

Analytical & Bioanalytical Electrochemistry

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Full Paper

Simultaneous Electrochemical Determination of Paracetamol, Dopamine and Diclofenac at Diacerein Modified Carbon paste Electrode: A Voltammetric Study

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Received: 24 June 2017 / Received in revised form: 7 August 2018 / Accepted: 9 September 2018 / Published online: 30 November 2018

Abstract- Diacerein was used for the modification of carbon paste electrode (CPE) to determine the electrochemical behavior of paracetamol (PA) in 0.2 M phosphate buffer solution (PBS) at pH 7. The effect of concentration, scan rate, pH and surfactant was studied for electrochemical studies of paracetamol. The Diacerein modified carbon paste electrode showed an excellent electrocatalytic activity for the selective determination of PA in the presence of Dopamine and Diclofenac by using CV and differential pulse voltammetric techniques (DPV) respectively. The catalytic peak current obtained was linearly related to PA concentrations in the ranges of to 0.1 mM to 0.6 mM with correlation co-efficient of 0.9981 which reveals the adsorption controlled process. The detection limit of paracetamol was found to be 3.8×10^{-6} M. The present technique provides a novel method for the simultaneous determination of Paracetamol, Dopamine and Diclofenac in their mixture sample.

Keywords- Paracetamol, Dopamine, Diclofenac, Diacerein, modified carbon paste electrode, Sodium alpha-olefin sulfonate Surfactant, Cyclic voltammetry

1. INTRODUCTION

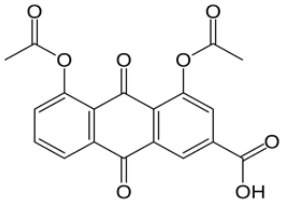
In recent years, efforts have been exerted in the development of voltammetric methods for the determination of Paracetamol (PA) and Dopamine (DA) in biological samples.

Paracetamol, (N-acetyl-p-aminophenol) known as acetaminophen, is a pain killer that is popular throughout the world because it is remarkably safe to the stomach. Paracetamol (PC) was firstly introduced into medicine as an antipyretic/analgesic by Von Mering in 1893. Prior to this cinchona bark, which was also used to make the anti- malaria drug quinine, had been used to treat fevers. paracetamol is one of the most commonly used analgesics in pharmaceutical formulations, for the reduction of fever and also as a pain killer for the relief of mild to moderate pain associated with headache, backache, arthritis and postoperative pain in adults and children. It is the most used medicine after acetylsalicylic acid in many countries as an alternative to aspirin and phenacetin [1-6].

Dopamine is one of the excitory neurotransmitters that play an important role in physiological events. It is involved in the functioning of renal, cardiovascular, hormonal and nervous systems. Dopamine is involved in neurological diseases such as Parkinson's [7], Alzheimer's disease [8] and schizophrenia [9-10]. As a result of these discoveries, catecholamines, and drugs are now widely used in the treatment of bronchial asthma, hypertension, Parkinson's disease, myocardial infarction and cardiac surgery. Consequently various approaches have been made to develop selective and sensitive methods for the determination of DA concentrations. Dopamine is an electrochemically active compound that can be directly oxidized at an appropriate potential and a suitable electrode material.

Diclofenac (DA) is a synthetic nonsteroidal anti-inflammatory drug (NSAID), has been proven as a safe and efficacious drug in the treatment of a variety of inflammatory and rheumatoid disorders [11]. Diclofenac is well absorbed after oral administration with extensive hepatic metabolism. This compound exhibits a terminal half-life of 1–2 h, volume of distribution of 0.17 l/kg, 99% protein binding and enters the synovial fluid [12]. The determination of small amounts of diclofenac in pharmaceutical preparations is very important for medical and pharmaceutical needs where it is used for the treatment of various diseases. Therefore it is vital to develop a simple, fast, selective and cost-effective method of determining the trace amounts of diclofenac in different pharmaceutical formulations.

In this study, the surfactant (sodium alpha olefin sulphonate) is used as a modifier for the electrochemical determination of Paracetamol. The term surfactant is derived from surface active agent and is a compound that contains a hydrophilic (attracted to water) and a hydrophobic (repelled by water) segments. Because of their unique molecular structures, surfactant has been extensively used in the fields of electrochemistry and electroanalytical chemistry [13-15] for various purposes. To improve the detection limits of some biomolecules Hu's group [16-18] has introduced surfactants to electroanalytical chemistry.
Diacerein, a purified compound with anthraquinonic structure, has been shown to inhibit, *in vitro and in vivo,* the production and activity of IL-1 and the secretion of metalloproteases without affecting the synthesis of prostaglandins [19-20].



Scheme 1. Structure of Diacerein

Diacerein is a drug with interleukin-1 (IL-1)–inhibitory activity developed for the treatment of osteoarthritis (OA).In animals, oral administration of diacerein resulted in anti-inflammatory activity as manifested by an inhibition of edema induced by the injection of carrageen an into the footpad. Diacerein inhibited adjuvant arthritis induced in rats by the injection of Mycobacterium tuberculosis. It also exhibited analgesic effects and antipyretic activities in animal models [21-22].

The aim of the work is to establish a simple and sensitive electrochemical method for the determination of Paracetamol in the presence of Diacerein and surfactant. Diacerein MCPE shows excellent electrocatalytic activity for the oxidation of Paracetamol, it accelerates the electron transfer rate and lowers the over potential. Some electrochemical parameters of Paracetamol electrochemical oxidation were measured by different electrochemical methods.

2. EXPERIMENTAL

2.1. Reagents and materials

Diacerein, Dopamine, Paracetamol, Diclofenac and Sodium alpha-olefin sulfonate were obtained from Himedia Chemicals. Perchloric acid, sodium dihydrogen orthophosphate dihydrate, and di-sodium hydrogen phosphate anhydrous were obtained from Merck. 25×10^{-4} M DA, 25×10^{-4} M PA, and 25×10^{-4} M DF stock solutions were prepared by dissolving in 0.1 M perchloric acid solution and double distilled water respectively. All other reagent solutions were prepared in double distilled water. All chemicals are of analytical grade quality and were used without further purification.

2.2. Apparatus and procedure

Electrochemical measurements were carried out with a CHI Model 660c Electrochemical Work station connected to a personal computer for control and data storage. All electrochemical experiments were performed in a standard three-electrode cell. The bare carbon paste electrode or the modified electrode used as a working electrode. The counter electrode was platinum wire and the reference electrode was a saturated calomel electrode (SCE). All potentials reported are with respect to the SCE.

2.3. Preparation of bare and modified carbon paste electrode

The bare carbon paste electrode was prepared by hand mixing of graphite powder and silicon oil at a ratio of 70:30 (w/w) in an agate mortar until a homogenous paste was obtained. The prepared carbon paste was tightly packed into a PVC tube (3mm internal diameter) and the electrical contact was provided by a copper wire connected to the paste in the end of the tube. Similarly the modified carbon paste electrode was prepared by grinding 8mg concentration of Diacerein along with graphite powder.

3. RESULTS AND DISCUSSION

3.1. Electrocatalytic Oxidation of paracetamol at Diacerein Modified Carbon Paste Electrode

The cyclic voltammograms of 1×10^{-4} M PA in 0.2 M PBS showed slightly shifted towards positive side with the increase in the oxidation current of diacerein modified carbon paste electrode as compared to the bare carbon paste electrode as shown in Fig. 1. The oxidation peak current enhancement of paracetamol at the Diacerien MCPE electrode was caused by the electrocatalytic effect.

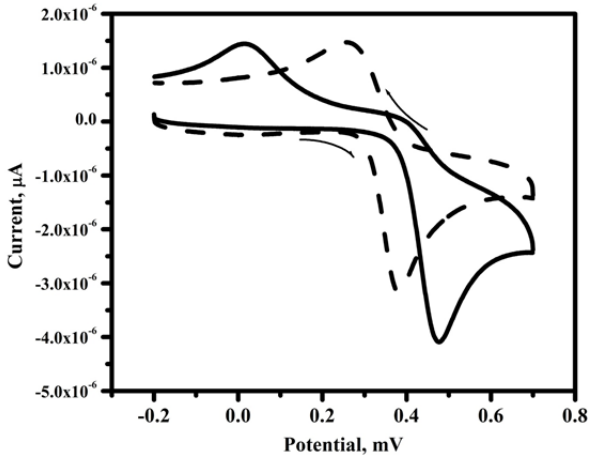


Fig. 1. Cyclic voltammograms obtained for the electrochemical response of PA at Diacerein MCPE (solid line) and bare carbon paste electrode (dashed line) in 0.2 M phosphate buffer solution pH 7.0 containing 0.1 mM PA scan rate 100 mV/s

3.2. Effect of scan rate

The effect of scan rate on 1×10^{-4} M PA was studied at Diacerien MCPE by using pH 7 of PBS as a supporting electrolyte with CV technique. Fig. 2A gives the information about the effect of scan rate on the peak currents and peak potentials. The peak current gradually increases with the increase in scan rates. In Fig. 2B and Fig. 2C gives the plot between scan

rate(ν) and square root of scan rate($\nu^{1/2}$) versus peak currents (I_{pc}), was found to be linear with a correlative coefficient(R^2)=0.9866 and (R^2)=0.9984.This indicating adsorption controlled process at the electrode surface [23].

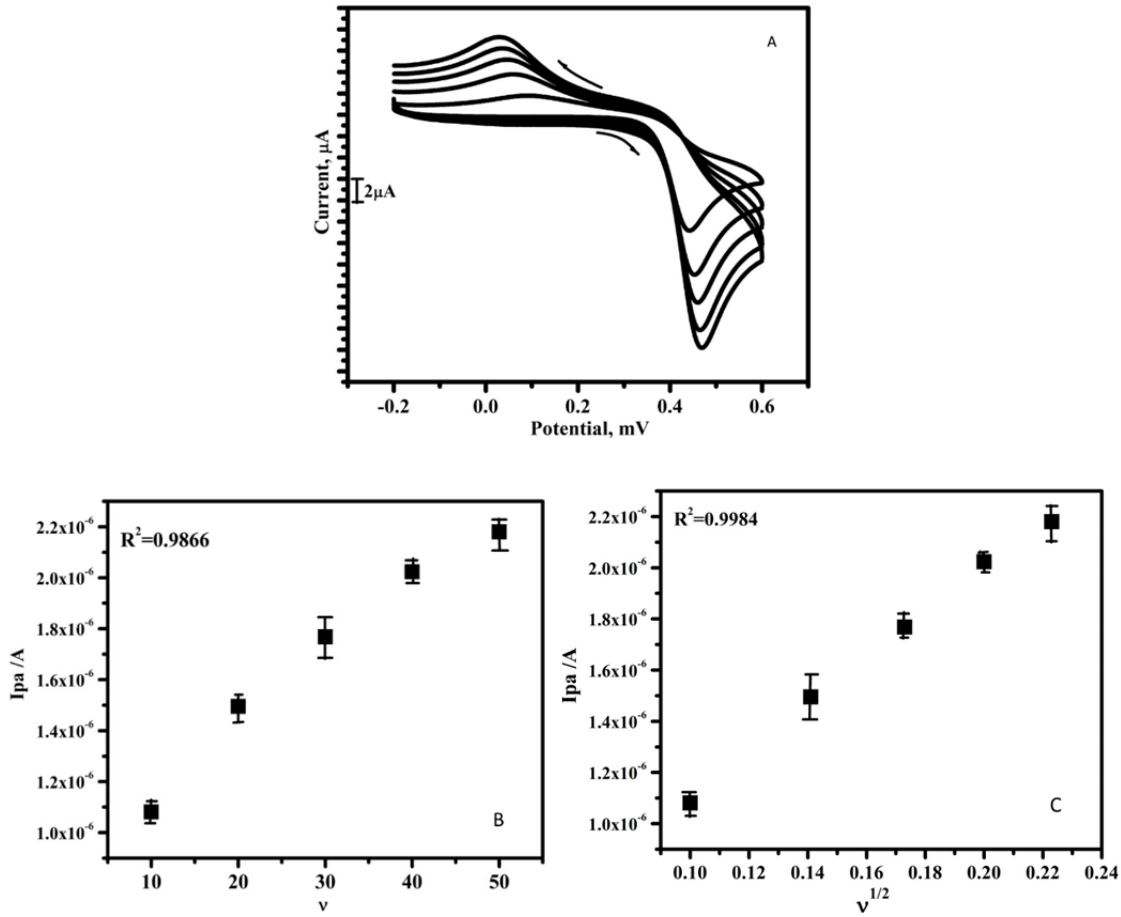


Fig. 2. A) Cyclic voltammogram of different scan rate in the presence of 0.1 mM PA at Diacerein MCPE in 0.2 M phosphate buffer solution at pH 7.0.scan rate 10 mV/s -50 mV/s; **B)** Plot of anodic peak current versus scan rate; **C)** Plot of anodic peak current versus square root of scan rate

3.3. The effect of pH

The effect of pH on the modified electrode with the oxidation peak potential was investigated by cyclic voltammetry of the solution containing 1×10^{-4} M PA in Fig. 3A. The E_{pa} versus pH graph clearly indicates that the catalytic peak shifts to a more negative potential with increase of pH. From the Fig. 3B, it could also be seen that the current reached the maximum at pH 7.0.

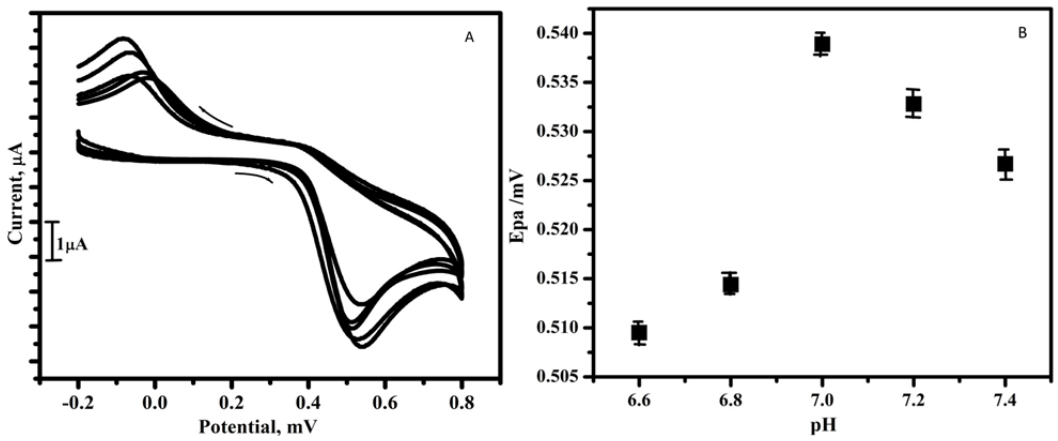


Fig. 3. A) Cyclic voltammograms of 0.1 mM PA for different pH (from 6.6 to 7.4 pH) at Diacerein MCPE; **B)** Plot of anodic peak potential versus pH

3.4. The effect of concentration of paracetamol

The effect of concentration of 1×10^{-4} M PA was studied at Diacerein MCPE in 0.2 M PBS of pH 7. Fig. 4A. From the figure it is clear that with increase in the concentration of PA the peak current increases. The plot of I_{pa} versus concentration of PA shows a linear relation with correlation coefficient of 0.9981 in Fig. 4B. The catalytic peak current has a linear relationship with PA concentration over the range of 0.1 mM to 0.6mM. The detection limit for PA was found to be 3.8×10^{-6} M and quantification limit was 1.28×10^{-7} M.

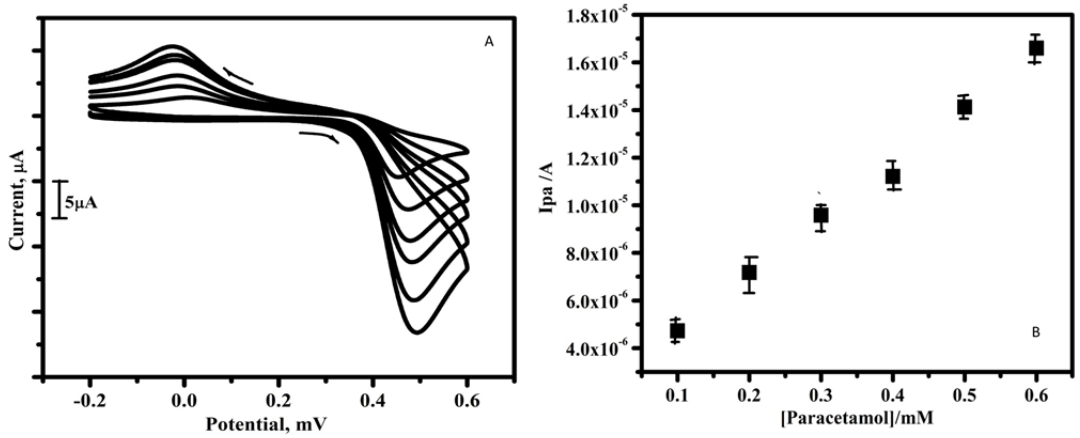


Fig. 4. A) Cyclic voltammogram of variation of concentration of paracetamol from 0.1 mM to 0.6 mM in presence of phosphate buffer solution at pH 7.0; **B)** Plot of anodic peak current versus the concentration of PA

The detection limit and quantification limit was calculated by using the formulas (1) and (2) [24–26] and the corresponding results were tabulated in Table 1, where S is the standard

deviation and M is the slope obtained from the three calibration plots. The comparison of this electrode with other modified electrode for the determination of PA is listed in Table 1.

$$LOD = 3S/M \quad (1)$$

$$LOQ = 10S/M \quad (2)$$

Table 1. Comparison of the performances of paracetamol electrochemical sensors

Modified electrodes	pH	Detection limit (M)		Ref.
Graphene/GCE	9.3	3.2×10^{-8}		[28]
PAY/nano-TiO2/GCE	7.0	2.0×10^{-6}		[29]
MWCNT-BPPGE	7.5	1.0×10^{-8}		[30]
C60/GCE	7.2	0.5×10^{-4}		[31]
PANI-MWCNTs/GCE	5.5	2.5×10^{-7}		[32]
C–Ni/GCE	3.0	6.0×10^{-7}		[33]
Nafion/TiO2–graphene/GCE	7.0	2.1×10^{-7}		[34]
Diacerein/MCPE	7.0	3.8×10^{-6}		[This work]

3.5. Electrochemical response of paracetamol at carbon paste electrode on to the surface with Sodium alpha olefin sulphonate

The electrochemical response of paracetamol at carbon paste electrode was shown in Fig. 5 with 0.2 M PBS of pH 7.0. Owing to the roughness of the electrode surface, the cyclic voltammogram of paracetamol in bare carbon paste electrode (solid line) and Diacerein modified carbon paste electrode the absence of SAOS is low signal (dashed line).

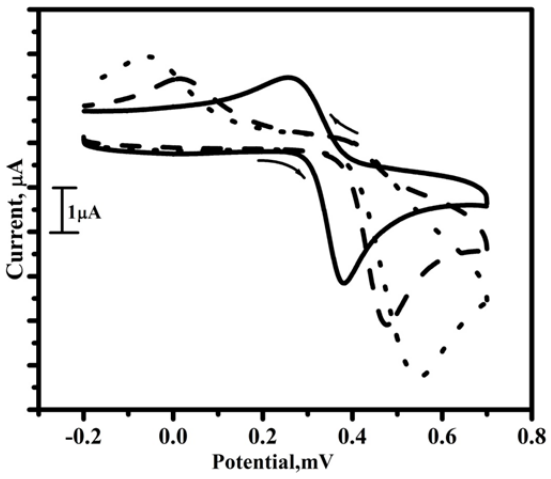


Fig. 5. Cyclic voltammogram of 0.1 mM PA at BCPE (solid line), Diacerein MCPE (dashed line), and 50µM SAOS on the modified CPE (dotted line) in 0.2 M phosphate buffer solution pH 7.0. scan rate 100 mV/s

However, the voltammetric response is apparently improved in the presence of 50µL of SAOS, reflected by the enlargement of anodic peak current (i_{pa}) (dotted line). The probable mechanism is the SAOS surfactant molecule diffuses into the carbon paste electrode along with the paracetamol results increase in the signal [27].

3.6. Simultaneous determination of PA and DA

Diacerein modified carbon paste electrode was introduced for analysis of PA in the containing DA. The sample mixture concentrations were 1×10^{-4} M PA and 1×10^{-4} M DA in PBS of pH 7. As shown in Fig. 6, the voltammogram obtained for the mixture of sample at BCPE (dashed line) was less sensible the oxidation peaks as while two separated well-defined oxidation peaks can be found at Diacerein MCPE (solid line).The anodic peak potentials located around at 520 and 220 mV for PA and DA respectively. The difference of the Epa for PA-DA was 300 mV by CV.

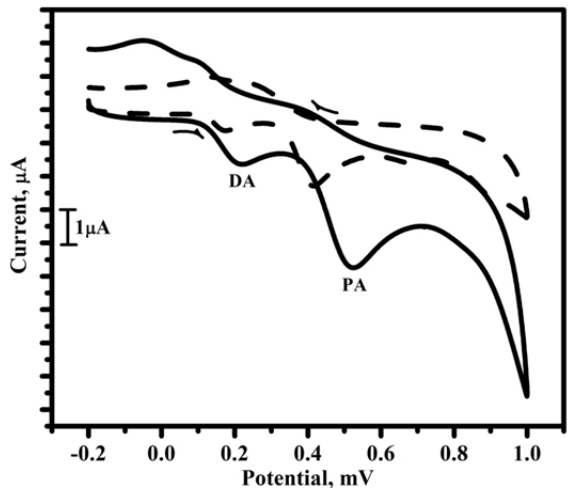


Fig. 6. Cyclic voltammograms recorded containing mixture of PA and DA at bare CPE (dashed line) and Diacerein MCPE (solid line) in 0.2 M PBS pH 7.0 at scan rate 100 mV/s

3.7. Influence of PA, DA and DF on each other

Fig.7A shows the DPVs obtained by increasing the concentrations of DA (from 0.2 mM - 0.5 mM) in the presence of 0.2 mM PA and 0.2 mM DF. An increase in the peak current of DA was observed with the increasing DA concentration and the voltammetric peak of PA and DF was almost unaltered during the oxidation of DA.

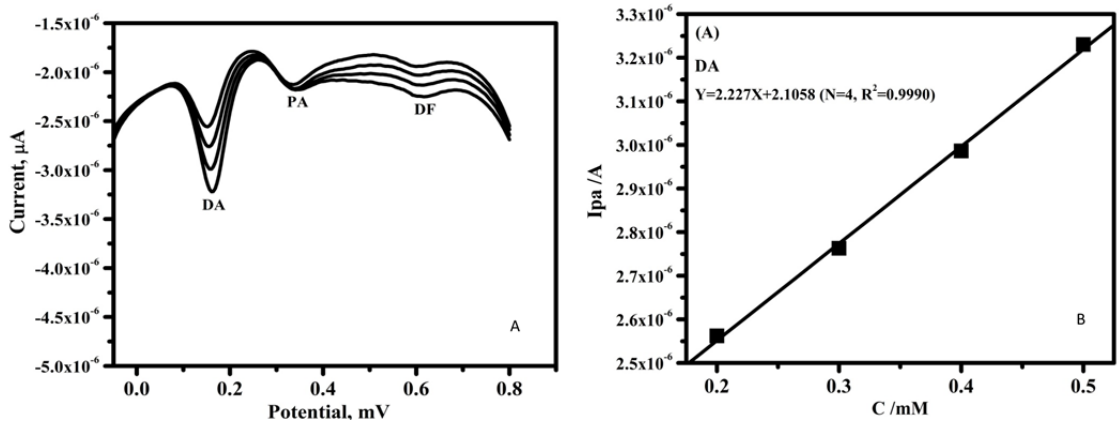


Fig. 7. A) Differential pulse voltammograms of DA (0.2 mM, 0.3 mM, 0.4 mM, 0.5 mM) in 0.2 M phosphate buffer solution of pH 7.0 in the presence of 0.2 mM PA and 0.2 mM DF at Diacerein MCPE with the scan rate of 100 mV/s; **B)** The plot shows anodic peak current (I_{pa}) versus DA concentration

Similarly in Figs. 8A and 9A self explains the concentration effect of PA from 0.2 mM to 0.5 mM and DF from 0.2 mM to 0.5 mM respectively. These results shows that the DA, PA and DF were exist independently in their mixtures of samples. The corresponding graphs of anodic peak current versus various concentrations of DA(0.2 mM-0.5 mM), PA(0.2 mM-0.5 mM), DF(0.2 mM-0.5 mM) showed linear relationships with linear regressions for A (DA) I_{pa} (µA)=2.227 Cm M L^{-1}+2.10, B (PA) I_{pa} (µA)=7.6 Cm M L^{-1}+2.089, C(DF) I_{pa} (µA)=4.36 Cm M L^{-1}+2.154, the correlation coefficient for these linear graphs was 0.9990, 0.9913 and 0.9009 respectively for this Diacerein MCPE and the detection limit for PA was found to be 2.4×10^{-6} M which were shown in Figs., 7B, 8B and 9B respectively.

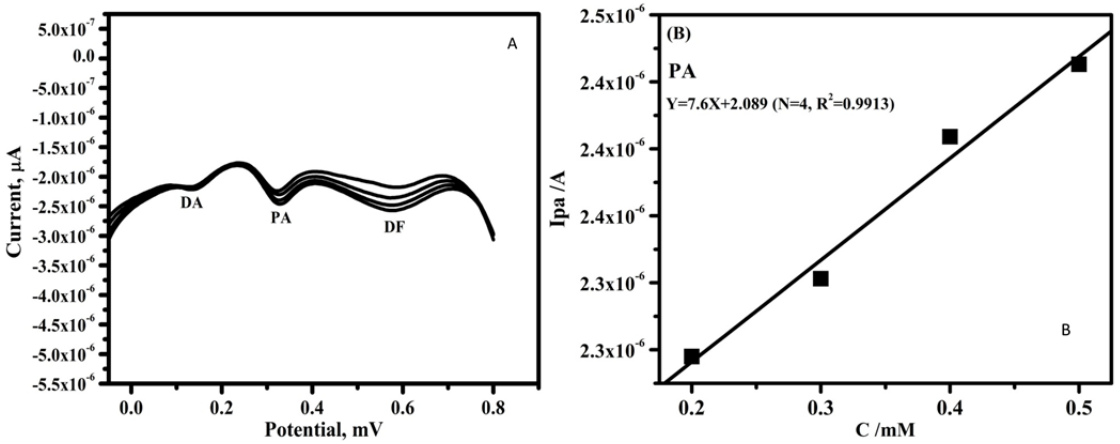


Fig. 8. A) Differential pulse voltammograms of PA (0.2 mM, 0.3 mM, 0.4 mM, 0.5 mM) in 0.2 M phosphate buffer solution of pH 7.0 in the presence of 0.2 mM DA and 0.2 mM DF at Diacerein MCPE with the scan rate of 100 mV/s; **B)** The plot shows anodic peak current (I_{pa}) versus PA concentration.

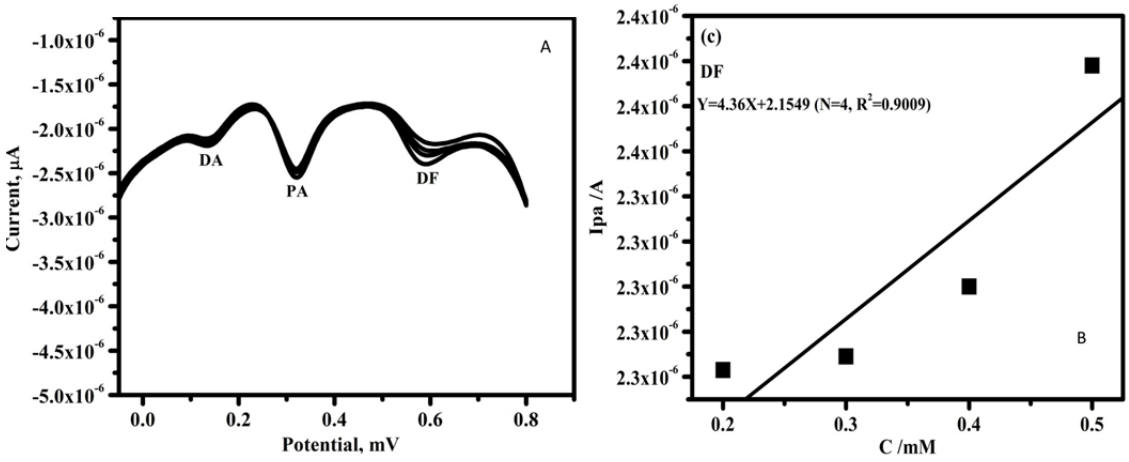


Fig. 9. A) Differential pulse voltammograms of DF(0.2 mM, 0.3 mM, 0.4 mM, 0.5 mM) in 0.2 M phosphate buffer solution of pH 7.0 in the presence of 0.2 mM DA and 0.2 mM PA at Diacerein MCPE with the scan rate of 100 mV/s; **B)** The plot shows anodic peak current (Ipa) versus DF concentration

4. CONCLUSION

In this work, the modified diacerein carbon paste electrode was shows electrochemical sensor for electrochemical determination of PA. The prepared modified electrode has detection limit of 3.8×10^{-6} M and it shows excellent sensitivity, selectivity and anti-fouling properties. The surfactant (sodium alpha olefin sulphonate) is used as a modifier showed have made better sensor for the detection of PA. Moreover, valid response to paracetamol and the good potential separations obtained for DA, PA and DF are prospective pointers to the application of this sensor to other biological molecules as well.

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