

Poly (L-leucine) modified carbon paste electrode as an electrochemical sensor for the detection of paracetamol in presence of folic acid

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ABSTRACT

Here, L-leucine based electrochemical sensor was designed for the simultaneous analysis of paracetamol (PA) and folic acid (FA). Electropolymerization of L-leucine was carried out on the surface of the carbon paste electrode (CPE). The electrochemical deeds of the biomolecules were explored through cyclic voltammetry (CV) and differential pulse voltammetry (DPV) at the fabricated sensor. The invented poly (L-leucine) modified carbon paste electrode (PLCN-MCPE) showed very good interaction with the analyte molecules which results in the significant determination of PA and FA in terms of sensitivity and selectivity. The electrochemical reaction mechanism between the surface of the developed sensor and the analytes was carried out in terms of effects of scan rate, concentration, and the electrode process was found to be adsorption-controlled. The kinetics such as the number of electron transfer (n) and the heterogeneous rate constant (k_0) were defined for PA and FA at MCPE. The lower limit of detection for PA and FA were assessed to be 0.44 and 2.4 μM correspondingly. As well, the availability of the sensor in real-world sample analysis was also investigated with satisfactory results.

1. Introduction

The availability of medicine without the prescription of the medical advisors' intake by the patient/peoples is quite common among the developing countries as self-medication. The common problems such as headache, cough, and fever were easily medicated by widespread known drugs among the masses such as aspirin, paracetamol (N-acetyl-P-aminophenol, or Acetaminophen) and folic acid (vitamin M or vitamin B₉) tablets. Paracetamol is an analgesic drug effectively used as a pain killer in the treatment of fever was consumed by irrespective of the age groups who were sensitive to aspirin as well [1–3]. It is believed that the side effects caused by the consumption of PA are quite less; however, the over dosages may lead to some serious disorders related to kidney and liver [4–8]. Besides, folic acid (FA) is one of the essential nutrients used for women especially during pregnancy [9–10]. During the metabolism process, FA undergoes single electron transfer reactions and plays a momentous role during the synthesis of purines and pyrimidines [11]. The deficiency of FA causes some major disorders especially in children and adults such as heart diseases and

cancer [12]. Therefore, the investigation of precise technology is highly essential for the analysis of PA and FA. As of now, several different methods have been investigated by the researchers' for the analysis of FA and PA based on fluorimetry [13], capillary electrophoresis [14–15], high-performance liquid chromatography [16–19], spectrophotometry [20–23], titrimetry [24–32]. The short comes of these methods lies in their time consumption, expensive material preparation, and rigorous test pre-treatment steps. However, the electrochemical methods have received enormous interest due to its sensitivity; less expensive besides this they are more convenient for sample preparation, high selectivity for analytes, and stability [33–39]. In this work, we employed carbon paste electrode due to its excellent conductivity, stability, and the availability of large surface area [40–43]. Here, L-leucine is used as catalyst material, one of the important amino acids essential for metabolism in living cells as an electrode bio modifier to detect PA and FA. The use of poly (L-leucine) modified electrode exhibits significant catalytic behavior under electrolytic conditions, and here we used this as a modified electrode to evaluate the simultaneous sensing of FA and PA and the available kinds of literature in this area were minimal [44–45].

The proposed research suggests the simultaneous detection of PA and FA at fabricated PLCN-MCPE sensor, maintaining the physiological pH. Different electrochemical parameters like sweep rate,

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concentration, simultaneous study, interference, and stability were examined including real sample analysis. The proposed sensor exhibited satisfactory catalytic behavior among all the parameters concerning the fortitude of PA and FA independently and concurrently.

2. Experimental

2.1. Materials

The chemicals and reagents utilized in this research were sourced locally and employed as received. Folic acid, paracetamol (Merck, India), and their stock solution (0.25 μM) were prepared in aqueous 0.1 M NaOH and deionized water, respectively. The optimized PBS (phosphate buffer solution) was made using disodium hydrogen phosphate and sodium dihydrogen orthophosphate. The graphite powder having a dimension less than 50 μm was procured from Merck and paraffin oil having density 0.88 gcm^{-3} was purchased from Fluka. Moreover, L-Leucine was purchased from Himedia chemicals, India.

2.2. Methods

The electrochemical considerations were monitored in a standard electrochemical terminal called CH Instruments-model CHI 660C, USA. The workstation consists of a conventional cell having three electrodes set up in which BCPE and PLCN-MCPE was applied as a working electrode, saturated calomel electrode as a reference electrode, and the platinum electrode a counter electrode correspondingly.

3. Results and discussion

3.1. Electropolymerization of L-leucine on BCPE

The process of L-leucine electropolymerization on the surface of BCPE was done by considering 1 mM of L-leucine in the cell consists of 0.1 M NaOH as supporting media having the scan rate 50 mVs^{-1} (Fig. 1). The potential applied was in the range of -0.5 to 0.4 V for ten repetitive polymerization cycles. Here we can notice the linear reliance of peak current with the polymerization cycle that gives a clue about the establishment of a polymeric film on the CPE surface [46]. Later, the influence of different polymerization cycles (5 to 25) on the CPE plane was investigated, and the resultant peak current for PA (0.1 $\times 10^{-4}$ M) was recorded

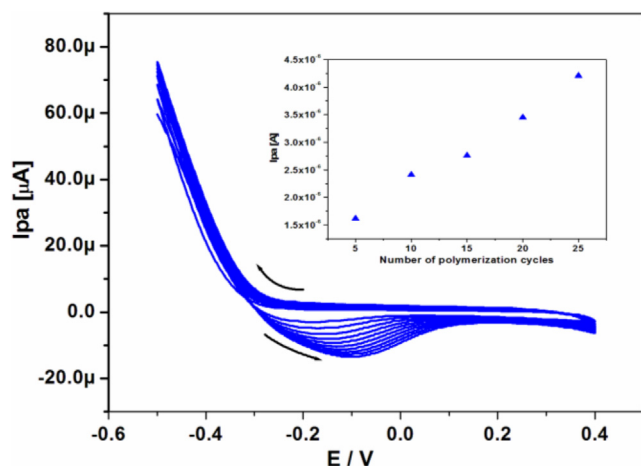


Fig. 1. CV curves for the electropolymerization of 1 mM L-leucine, inset anodic peak current (I_{pa}) for multiple cycles.

(Fig. 1 inset). The peak current of PA exhibited linear dependence with different polymerization cycles. Finally, ten polymerization cycles were chosen for the modification of CPE through the electropolymerization process.

3.2. Sensing behavior of poly (L-leucine)/MCPE towards PA

The electrocatalytic behavior of poly (L-leucine) MCPE towards PA was studied by CV and DPV techniques. Fig. 2 demonstrates the CV's of 0.1 $\times 10^{-4}$ M PA at BCPE (scattered row) and PLCN-MCPE (hard row) using 0.2 M PBS (pH 7.4) as supporting media having the scan rate 50 mVs^{-1} . An inadequate redox electrochemical response was obtained for PA at BCPE and the potential separation (ΔE_p) to be 0.10 V. On the other hand, PLCN-MCPE exhibits a considerable enrichment in redox peak current and ΔE_p was estimated at 0.07 V. A known factor that ΔE_p is a function of pace of electron transfer, lesser the ΔE_p value privileged will be the electron transfer pace [47]. Hence, the outstanding development concerning the electrochemical fortitude of PA has happened at PLCN-MCPE.

Fig. 3a depicts the CV curves of 0.1 $\times 10^{-4}$ M PA at dissimilar scan rates with the incidence of 0.2 M PBS as supporting media. The outcome predicts that the redox peak current of PA is linearly dependent on the scan rate (10–100 mVs^{-1}) and the shift in peak potential might be due to quicker electron transfer at PLCN modified CPE. To probe the type of electrode route, anodic peak current (I_{pa}) versus scan rate (ν) was recorded (Fig. 3b) that exhibited fine linearity $R^2 = 0.999$ (Linear regression equation: $I_{pa} (\mu\text{A}) = 4.323 \times 10^{-7} + 3.79 \times 10^{-8}$). Conversely, the relation between anodic peak current (I_{pa}) versus square root of scan rate ($\nu^{1/2}$) (Fig. 3c) was established with $R^2 = 0.993$ (Linear regression equation: $I_{pa} (\mu\text{A}) = 1.1021 \times 10^{-6} + 1.613 \times 10^{-5}$). Hence, the adsorption-controlled mass transfer reaction was recognized at the modified sensor. In addition to this, the number of electron transfer (n) and heterogeneous rate constant (k_o) of electrochemical oxidation of PA were evaluated using the equation (1) [48] and (2) [49], respectively and the obtained grades are presented in Table 1.

$$n = 90.6/\Delta E_p \quad (1)$$

$$k_o = \Psi \left[D_o \cdot \pi \cdot \nu \left(\frac{nF}{RT} \right) \right]^{\frac{1}{2}} \quad (2)$$

Where, Ψ is the degree of reversibility, ν is the scan rate and D_o is the diffusion coefficient

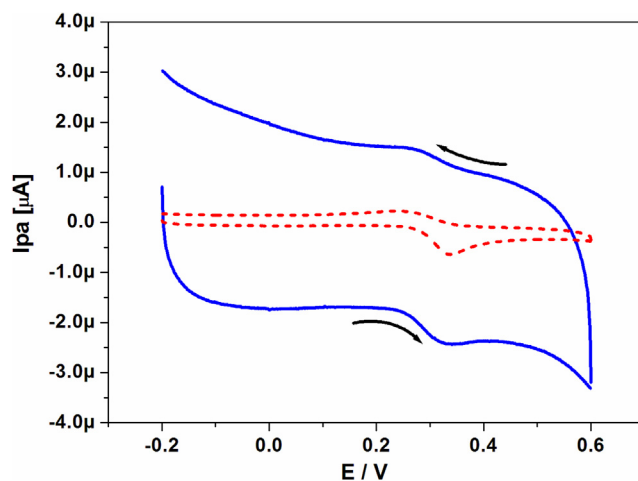


Fig. 2. CV's of 0.1 $\times 10^{-4}$ M PA at BCPE (scattered row) and PLCN-MCPE (hard row).

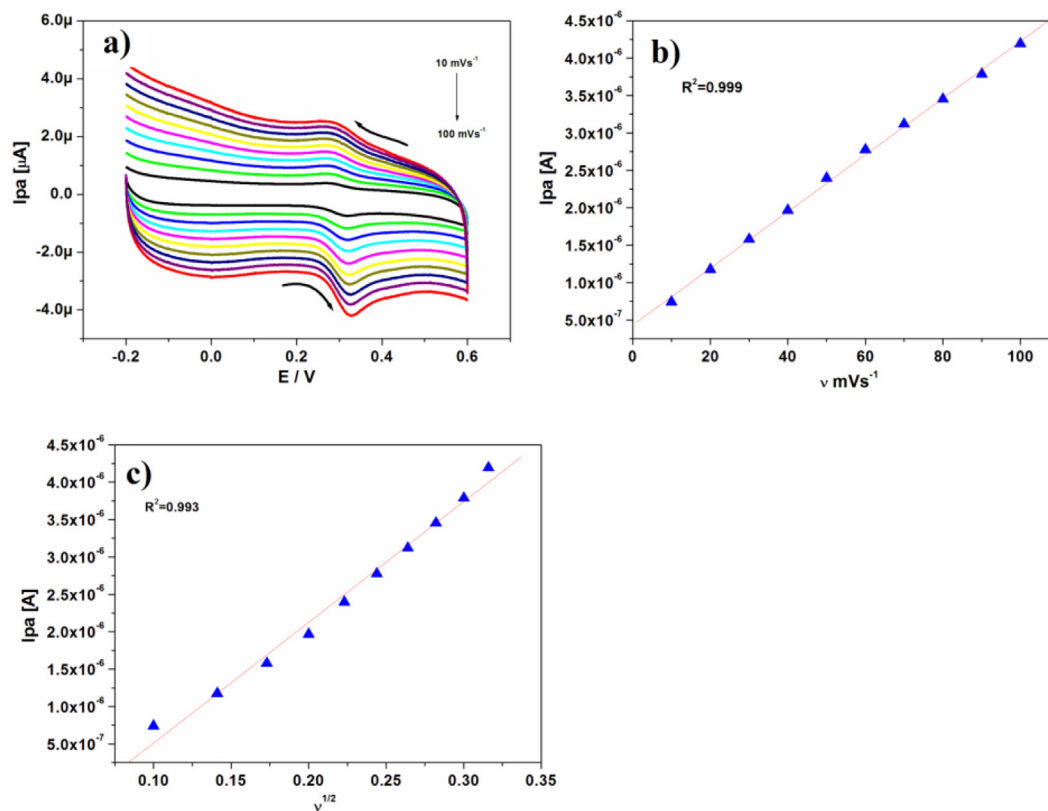


Fig. 3. a) CV's for 0.1×10^{-4} M PA at PLCN-MCPE with different scan rates ($10\text{--}100\text{ mVs}^{-1}$) b) plot of anodic peak current (I_{pa}) against scan rate (v), c) plot of anodic peak current (I_{pa}) against the square root of scan rate ($v^{1/2}$).

Table 1

The number of electron transfer (n) and heterogeneous rate constant (k_o) for PA at PLCN-MCPE.

Scan rate (mVs^{-1})	$\Delta E_p/\text{mV}$	Number of electron transfer (n)	The heterogeneous rate constant (k^0/s^{-1})
10	52	1.74	0.01
20	52	1.74	0.02
30	52	1.74	0.03
40	50	1.8	0.03
50	55	1.64	0.04
60	53	1.7	0.04
70	58	1.56	0.04

The redox behavior of PA at different concentrations was examined at PLCN-MCPE (Fig. 4a). The concentration of PA was speckled

from $0.2 - 0.9 \times 10^{-4}$ M employing 0.2 M PBS as supporting media and the scan rate was 50 mVs^{-1} . The appeared result suggests that the peak current of PA is linearly dependent on the concentration. In Fig. 4b, the linearity ($R^2 = 0.999$) was estimated by the plot of anodic peak current (I_{pa}) versus concentration. The lower detection limit (LOD) and the limit of quantification (LOQ) of PA was evaluated to be $0.44 \mu\text{M}$ and $14.7 \mu\text{M}$, respectively through the equation (3) and (4) [50–53].

$$\text{LOD} = 3S/M \quad (3)$$

$$\text{LOQ} = 10S/M \quad (4)$$

Where S denotes the standard deviation and M represents the slope.

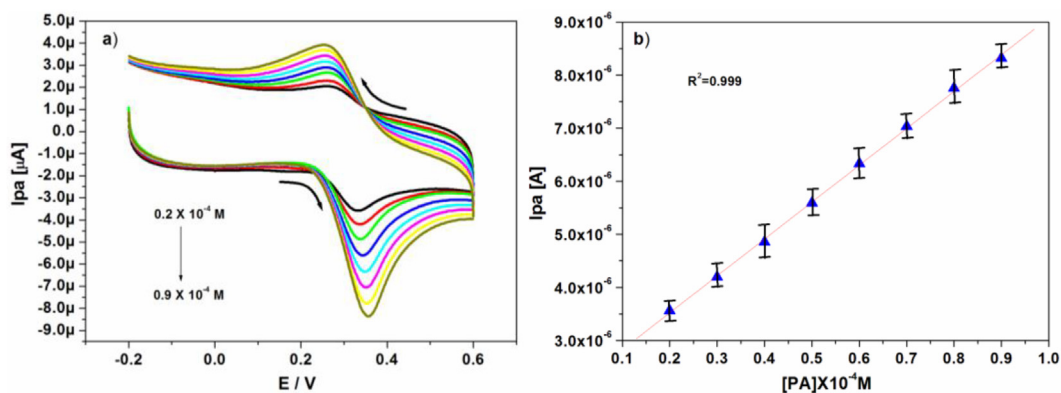


Fig. 4. a) CV's for PA at PLCN-MCPE with different concentrations (0.2 to 0.9×10^{-4} M), b) Plot of anodic peak current (I_{pa}) against the concentration of PA.

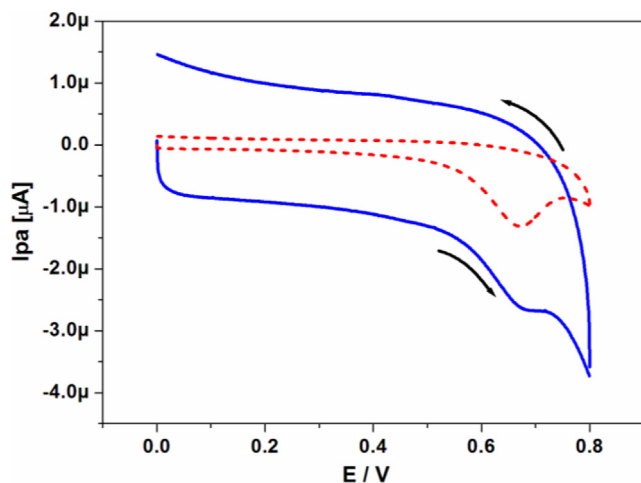


Fig. 5. CV curves obtained for 0.1×10^{-4} M FA at BCPE (scattered row) and PLCN-MCPE (hard row).

3.3. Sensing behaviour of poly (L-leucine)/MCPE towards FA

Like PA, the sensing behaviour of PLCN-MCPE towards FA was also examined. Fig. 5 demonstrates the CV signals obtained for 0.1×10^{-4} M FA at bare CPE (dotted line) and PLCN-MCP electrode (solid line) at the scan rate 50 mVs^{-1} . The CV of bare CPE exhibited a well-defined oxidation peak of FA with low response. Whereas, the electrochemical oxidation characteristic appeared at PLCN modified CPE was higher as compared to bare CPE that confirms the electrocatalytic role of polymeric film on the CPE surface. Thus, PLCN modified CPE electrode sensor exhibited noteworthy sensing behaviour towards FA.

The scan rate effect (ν) on the kinetics of the electrode reaction and the type of electrode process was monitored at PLCN-MCPE.

Table 2

The number of electron transfer (n) and heterogeneous rate constant (k_0) for FA at PLCN-MCPE.

Scan rate (mVs^{-1})	Peak potential (E_p)	The heterogeneous rate constant ($\text{k}^0 \text{s}^{-1}$)
20	0.65	0.05
30	0.66	0.06
40	0.67	0.07
50	0.68	0.08
60	0.68	0.08
70	0.69	0.09
80	0.69	0.10

Fig. 6a shows the CV curves recorded for 0.1×10^{-4} M FA at dissimilar scan rates ($20\text{--}80 \text{ mVs}^{-1}$). The magnitude of peak current (I_{pa}) of FA gradually augmented with scan rate evidence the discrepancy of the kinetics of FA oxidation on a polymeric film of leucine. On the other hand, the linearity relationship among anodic peak current (I_{pa}) and scan rate (ν) was recorded in Fig. 6b which gave $R^2 = 0.999$. Also, the linear correlation between the anodic peak current (I_{pa}) and the square root of the scan rate ($\nu^{1/2}$) (Fig. 6c) was elucidated ($R^2 = 0.991$) and the adsorption-controlled mass transfer was confirmed. Besides, the quantity of electron transport (n) and heterogeneous charge constant (k_0) were evaluated for the electrochemical oxidation of FA using the equation (5) [49] and (6) [54] respectively and tabulated in Table 2.

$$i_p = 2.99 \times 10^5 n(\alpha.n)^{\frac{1}{2}} A.D_o^{\frac{1}{2}}.V^{\frac{1}{2}}C_o \quad (5)$$

$$i_p = 0.227nFAC_o k_0 \exp\{-\alpha.n_a f.(E_p - E_f)\} \quad (6)$$

Where, A elucidates the electrode surface area, C_o is the FA concentration and $f = F/RT$

Further, to gain more information about the PLCN modified CPE during the electro-oxidation of FA, the effect of concentration was analyzed. Fig. 7a illustrates the cyclic voltammetric response of FA

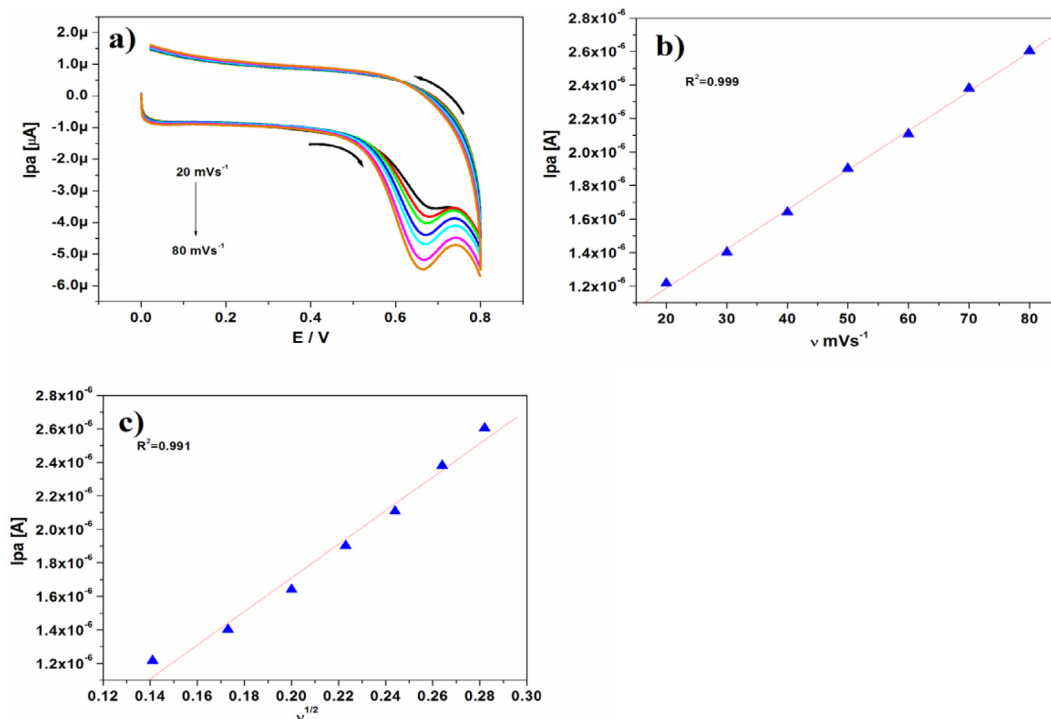


Fig. 6. a) CV's for 0.1×10^{-4} M FA at PLCN-MCPE with different scan rates ($20\text{--}80 \text{ mVs}^{-1}$), b) Plot of anodic peak current (I_{pa}) against scan rate (ν), c) Plot of anodic peak current (I_{pa}) against the square root of scan rate ($\nu^{1/2}$).

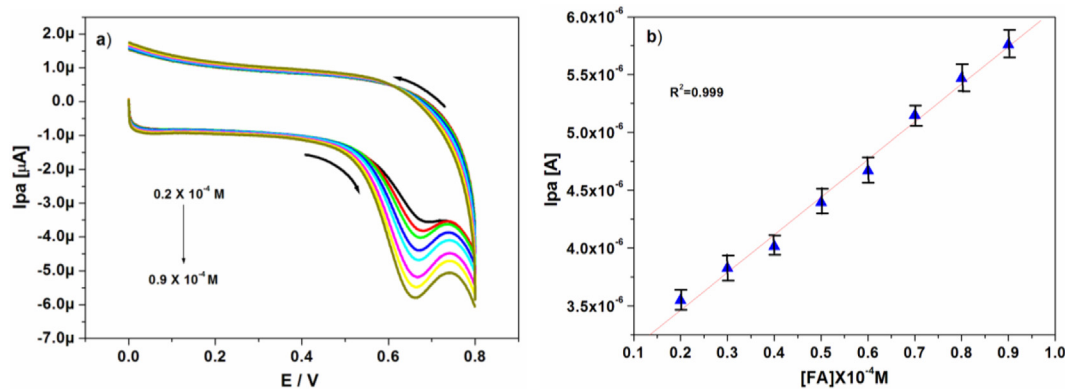


Fig. 7. a) CV curves gained for FA at PLCN-MCPE with different concentrations (0.2 to 0.9×10^{-4} M), b) Plot of anodic peak current (I_{pa}) against the concentration of FA.

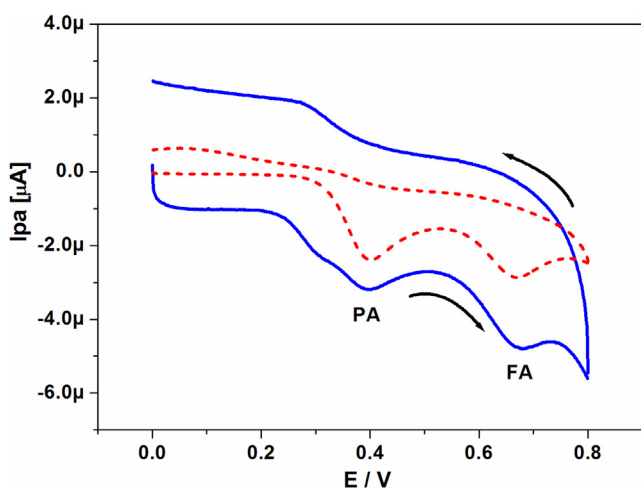


Fig. 8. CV's achieved for the mixture of PA (0.1×10^{-4} M) and FA (0.1×10^{-4} M) at bare (scattered row) and PLCN-MCPE (hard row).

at the PLCN-MCP electrode during the successive addition of FA concentration (0.2 – 0.9×10^{-4} M). The oxidation peak current enlarged sharply at every stage with the addition of FA concentration, and the linear correlation ($R^2 = 0.999$) was determined with the help of Fig. 7b. Moreover, by the equation (3) and (4), LOD and LOQ of FA was estimated to be $2.4 \mu\text{M}$ and $81.3 \mu\text{M}$, respectively.

3.4. Simultaneous electrochemical sensing of PA and FA at poly (L-leucine) MCPE

Using cyclic voltammetry, mixtures of PA and FA were determined at MCPE. Fig. 8 portrays the CV curves attained for the assortment of 0.1×10^{-4} M PA as well as 0.1×10^{-4} M FA at clean CPE (scattered row) and PLCN-MCP electrode (hard row) in the occurrence of 0.2 M PBS (pH 7.4) on the scan rate of 50 mVs^{-1} . At BCPE, two fine distinct oxidation peaks for PA and FA have emerged at potential 0.41 and 0.67 V respectively, whereas PLCN-MCPE illustrates the fortification in redox peak current along with the peak to peak partition (PA-FA) of 0.25 V that evidences the catalytic manners of the customized sensor in the simultaneous study.

3.5. Interference analysis

Fig. 9a demonstrates the DPV curves gained for the binary fusion of PA with FA, in which the concentration of PA was speckled, even as the concentration FA was kept at a predetermined concentration. The intensity of the peak current and the potential of PA progressively enlarged by escalating the concentration, whereas no alteration in peak potential was observed at invariable analyte (FA). A similar process was repeated for FA by maintaining the concentration of PA constant (Fig. 9b). Therefore, the tailored sensor exhibited admirable selectivity concerning the sensing of PA and FA.

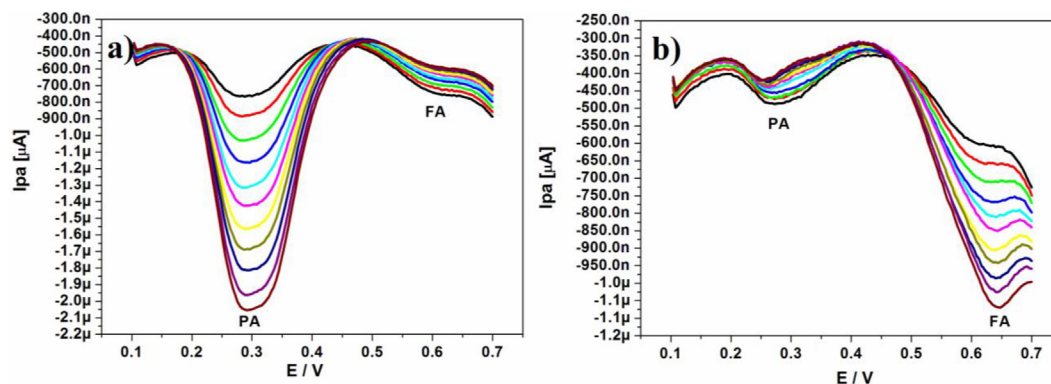


Fig. 9. a) DPV's achieved for PA with different concentration (20 – $120 \mu\text{M}$) in the presence of FA ($100 \mu\text{M}$) at PLCN-MCPE b) DPV's of FA with different concentration (100 – $600 \mu\text{M}$) in the presence of PA ($50 \mu\text{M}$) at PLCN-MCPE.

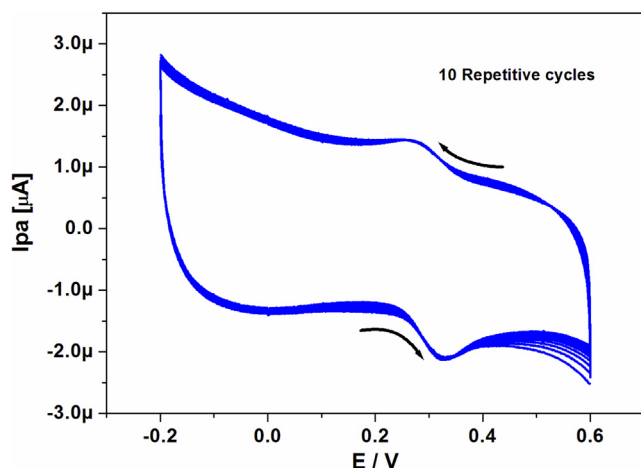


Fig. 10. Repetitive CV's recorded for 0.1×10^{-4} M PA at PLCN-MCPE.

Table 3
Real sample analysis of PA at PLCN-MCPE.

Sample	Content	Added (mM)	Found (mM)	Recovery
Tablet	5 mg	0.4	0.37	94.6%
Tablet	5 mg	0.5	0.48	96%
Tablet	5 mg	0.6	0.54	91%

Table 4
Real sample analysis of FA at PLCN-MCPE.

Sample	Content	Added (mM)	Found (mM)	Recovery
Tablet	5 mg	0.4	0.39	97.8%
Tablet	5 mg	0.5	0.47	94.1%
Tablet	5 mg	0.6	0.51	86.5%

3.6. Analytical applications

The electrochemical recognition of PA, as well as FA in the commercial tablets was investigated to discern the aptitude of the developed sensor in real-world sample analysis. From the voltammetric signals, the recovery test was examined utilizing the standard addition method [55] and the attained upshot for PA and FA were depicted in the Tables 3 and 4 respectively.

3.7. Stability of the fabricated sensor

The stability of the fabricated sensor (PLCN-MCPE) was scrutinized via the cyclic voltammetric process. Fig. 10 reveals the repetitive CV curves achieved for 0.1×10^{-4} M PA in the existence of 0.2 M PBS (pH 7.4) along with the scan rate of 50 mVs^{-1} (10 repetitive cycles). From the investigational outcome, the performance of the PLCN-MCPE endures for elongated period devoid of any amendments in their redox peak potential and current right through the electrochemical reaction which confirms the constancy of tailored sensor.

4. Conclusion

L-leucine is used as a catalyst material, and the tailored sensor (PLCN-MCPE) was engaged for the synchronized electrochemical sensing of PA and FA by CV as well as DPV methods. The customized electrode exhibited elevated sensitivity and selectivity

towards the detection of PA in the presence of FA. The number of electron transfer (n) and the heterogeneous rate constant (k_0) was also verified for PA and FA at MCPE. The mass transfer of the PLCN-MCPE was examined and established as adsorption-controlled. The lower detection limits (LOD) of PA and FA at the PLCN-MCPE was evaluated. The PA and FA were determined in the tablet sequentially to examine the capability of the MCPE. The anticipated electrode (PLCN-MCPE) exhibits incredible electrocatalytic response and can be appropriate for the simultaneous electrochemical sensing of PA and FA.

CRediT authorship contribution statement

T.S. Sunil Kumar Naik: Conceptualization, Investigation, Writing - original draft. **B.E. Kumara Swamy:** Conceptualization, Supervision, Writing - review and editing, final decision. **Praveen C. Ramamurthy:** Formal analysis, Writing and editing. **K. Chetankumar:** Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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