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Research Article

Development of a Sensitive Electrochemical Sensor for the Simultaneous Detection and Quantification of Acetaminophen Traces Using a Carbon Paste Electrode Modified with Black Carbon and $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ Nanoparticles

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ABSTRACT: Recently, the development of an advanced electrochemical sensor has received significant attention in the field of drug monitoring. The $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ (LSCF) nano-sized oxides were synthesized by a simple sol-gel citrate method, modified with black carbon (BC) and prepared as a carbon paste electrode (CPE) for the simultaneous determination of paracetamol (PCM) traces in PBS electrolyte through cyclic voltammetry (CV), differential pulse voltammetry (DPV) and electrochemical impedance spectroscopy (EIS) as sensing techniques. X-ray diffraction (XRD), scanning electron microscopy (SEM), and Ferrocyanide tests were used as characterization techniques. The calculated crystallite size *d*, was found to be 208.317 nm by XRD and 65.05 nm by SEM analysis. In conclusion, the modified prepared sensor LSCF/BC/CPE demonstrates a very satisfactory response, sensitivity, and selectivity towards PCM molecules compared with literature with a very low detection limit of 36 nM, high sensitivity of 75 $\mu A.\mu M^{-1}.cm^{-2}$, with a wide linear range from 0.1 µM to 180 µM by DPV technique. The modified LSCF/BC/CPE sensor demonstrated excellent results in the real pharmaceutical samples with a very good recovery of 94.56 % and a satisfactory relative standard deviation of 3.26 %.

Keywords: *Sensor, Nanoparticles, Black carbon, Paracetamol, Cyclic voltammetry, Differential pulse voltammetry.*

1 INTRODUCTION

Drugs traces determination in biofluids (blood, urine, serum, sweat, etc.), using newly developed sensors made of porous highly sensitive nanoparticles, especially with their application in advanced electrochemical techniques, is a crucial step in the field of drug quality control [1-3]. Paracetamol, also known as PCM, acetaminophen, or N-acetyl-p-aminophenol (as chemically illustrated in Scheme 1), is the key active ingredient of many analgesics and antipyretic medicinal formulations, commonly used for the alleviation of different symptoms like fever, headache, cough, cold, migraine and various types of chronic pain. PCM acts as an analgesic by inhibiting the synthesis of prostaglandins in the central nervous system and relieves fever through the hypothalamic heat regulation

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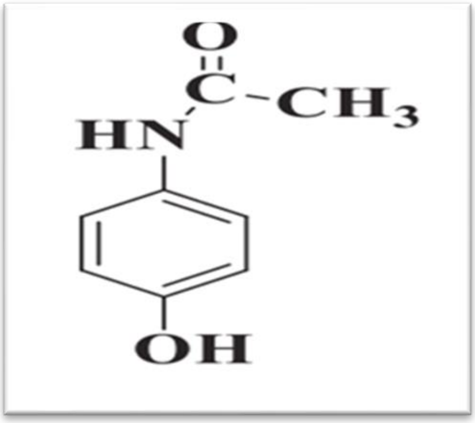
center [4]. Generally, acetaminophen does not have any harmful side effects, but its hypersensitivity or chronic use, also PCM overdoses can lead in some cases to the formation of certain hepatic and nephrotoxic metabolites which can result in kidney and liver failure [5]. Therefore, it is crucial to develop a new low-cost, highly effective, sensitive, and consistent sensor for the simultaneous sensing of paracetamol drug. Sensors made with metal nanoparticles are known as one of the most effective catalysts in many organic and electrochemical applications due to their excellent performance back to the high reactivity induced by their high active surface area and the small porous nano-sizes [6-8]. So far, several studies have reported on the study of PCM drugs with various analytical techniques mainly including spectrophotometry [9], flow injection chemiluminometry [10], thin layer chromatography [11], and high-performance chromatography [12]. Unfortunately, most of these conventional methods have several disadvantages related to low reproducibility, high instrument cost, complicated, and long time-consuming nature [13]. Developed electrochemical techniques especially cyclic voltammetry [13], differential pulse voltammetry [14], and electrochemical impedance spectroscopy have recently drawn a very useful approach overall these methods for PCM and other compound detection [15, 16]. Because they offer cheaper, highly sensitive and selective, low detection limits, and safe and simple analysis. The use of excellent new modified electrodes like carbon nanotubes (CNTs) or CPEs with good electrical conductivity, high electro-catalytic activity, and low detection limits is a very important step in the fabrication of high-performance electrochemical sensors [17-20]. Recently, different researchers studies have been reported the electrochemical detection of PCM molecules with carbon paste electrodes, such as: $MnFe_2O_4$ and $CoFe_2O_4$ nanoparticles modified graphite paste electrode GPE [21], Stevensite-modified carbon paste electrode (Stv-MCPE) [22], zirconium oxide ZrO_2 nanoparticles on modified CPE [23], imidazolium ionic liquid crystal on carbon paste composite (ILC/CPE) [24], magneto gold nanoparticles on CPE (Au NPs /Fe_3O_4/CPE) [25], La_2NiO_4 and Pr_2NiO_4 nano particles on CPE [26], polymerized L-phenylalanine modified carbon paste electrode (PLPAM/CPE) [27], poly(L-Leucine) layered carbon nanotube paste electrode [28], and 2,2 -[1,2 butanediylbis(nitriloethylidyne)]-bis-hydroquinone and TiO_2 nanoparticles CPE [20].

Currently, no report is available on the simultaneous electrochemical detection of paracetamol drug with $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$/BC/CPE modified sensor. In this context, cheaper, highly selective, sensitive, and very low detection limit than literature was reported.



Scheme 1. Chemical structure of Paracetamol drug.

2 MATERIAL AND METHOD

2.1 Chemicals and reagents

$La(NO_3)_3.6H_2O$(≥99%),$Sr(NO_3)_2$(≥98 %), $Co(NO_3)_3.6H_2O$(≥99%), $Fe(NO_3)_3.9H_2O$ (≥98%), citric acid ($C_6H_8O_7/H_2O$)(≥99%) were purchased from Sigma-Aldrich for the synthesis of LSCF nanomaterials using the citrate method. Paracetamol (PCM) was purchased from the BIOPHARM laboratory (Algeria), and the pharmaceutical product was purchased from PHYSIOPHARM laboratories (Algeria). Black Carbon (BC) (≥99%), Ferricyanide $K_3[Fe(CN)_6]$, and Ferrocyanide $K_4[Fe(CN)_6]$(≥98%), Ethylene Glycol (99%) were obtained from Biochem Chemopharma and Sigma Aldrich. All the reagents were of analytical grade, stored at room temperature (25°C), and all the solutions were prepared by dissolving the specified quantities of each product in 0.1 mM phosphate buffer solution (PBS).

2.2 Preparation of the sensor

LSCF nanoparticles were synthesized by a simple citrate method; all the details are illustrated in [29, 30]. The modified LSCF/BC/CPE sensor was prepared by mixing an appropriate quantity of the $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ synthesized nanoparticles and black carbon powder at ¼ and ¾ (w/w) ratios. LSCF NPs and BC powders were grounded well to achieve a smooth blending. After that, the resulting powder was mixed with 2 to 3 drops of the viscus ethylene glycol gel until a black dough (paste) was formed [31]. The formed paste was transferred into a clean capillary glass tube (d = 0.9 mm; S = 0.073 cm^2) by pressing it with a metal rod at the bottom of the glass tube with attaching a platinum wire for electrical contact. Finally, the LSCF/BC/CPE was air-dried for 2-3 minutes approximately, and then polished using 5-micron alumina, rinsed with methanol, and dried well before experiments.

2.3 Electrochemical instrıments and measurements

The XRD diagrams were obtained with an XPERT-PRO diffractometer using the CuKα radiation (1.5406 Å) (France). The morphology and microstructure of the LSCF synthesized nanoparticles were studied using a scanning electron microscope with LEO EVO-40xVPtype (Turkey). All voltammetric analyses were performed in a Voltalab Potentiostat-Galvanostat PGZ-301, (Algeria), Gamry Interface 1010B (Gamry, USA) electrochemical analyzer, (Malatya, Turkey). Electroanalytical measurements were performed in a cell (BASi C3 Cell Stand) at room temperature with conventional three electrodes consisting of an LSCF-modified CPE (0.9 mm in diameter) as a working electrode, Platinum (Pt) as a counter electrode, and a saturated silver chloride (Ag/AgCl) as a reference electrode. The voltammetric measurements were performed in a potential scanning range between -200 mV to +900 mV (vs. Ag/AgCl). Cyclic voltammetry and DPV measurements for PCM monitoring were performed in a 0.1 mmol.L^{-1} phosphate buffer solution (PBS) pH 7.4 (3µM to 180 µM in CV, and 0.1 µM to 180 µM in DPV). The electrochemical impedance spectroscopy (EIS) spectra were recorded in the frequency range of 10^5 to 10^{-2} Hz. The operating conditions for DPV studies were: a step potential of 2.0 mV, a pulse size of 50 mV (vs. Ag/AgCl), a sample period of 0.2 s, a pulse time of 0.1 s, and an equilibrium time of 2 s.

3 RESULT AND DISCUSSION

3.1 X-Ray diffraction analysis

The purity, structural characteristics, and fundamental crystallographic parameters of the prepared NPs were investigated using X-ray diffraction analysis, indicating the presence of a single-phase for LSCF nano-oxide with perovskite-type [32-40]. The diffraction lines of the XRD patterns presented in Figure 1 (a) for our $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ synthesized nanoparticles were in great agreement compared with LSCF perovskite prepared in previous work [41] with a rhombohedral symmetry with space group of (R3CH). This indicates that LSCF NPs have a single pure phase and are composed only of the desired metals (La, Sr, Co, Fe). The structural parameters and refinement of LSCF perovskite were obtained using the Jana 2006 software. The main parameters are presented in (Table 1). The comparisons of the resulting XRD patterns of LSCF nanoparticles and the characteristic peaks (2θ) with hkl values are at 2θ = 24.07°, 32.91°, 40.53°, 47.34°, 53.29°, 58.61°, 69.13°, and 78.90° corresponding to hkl values (100), (110), (111), (200), (210), (211), (220), and (310), the obtained average size *d* was equal to 208.317 nm. LSCF NPs characterized by a pure phase, contain Co and La transition metals which are considered very good catalysts, and have a small and narrow particle diameter, these main characteristics increase their surface area and lead to a very weak concentration detection limit and improve their best performance in this work.

3.2 Scanning Electron Microscopy Analysis

Scanning electron microscopy (SEM) analysis is an excellent characterization tool that is used to describe the shape, morphology, structure, and micro and nanosize of materials [29, 30]. The LSCF NPs powder was examined

Table 1. Crystallographic main parameters of the synthesized LSCF nanoparticles.

Material	Lattice parameters (Å)				
	S.G	a = b	c	α=β=γ	Volume (Å^3)
LSCF	**$R3^{-}CH$**	**5.428**	**13.225**	**120°**	**60.799**

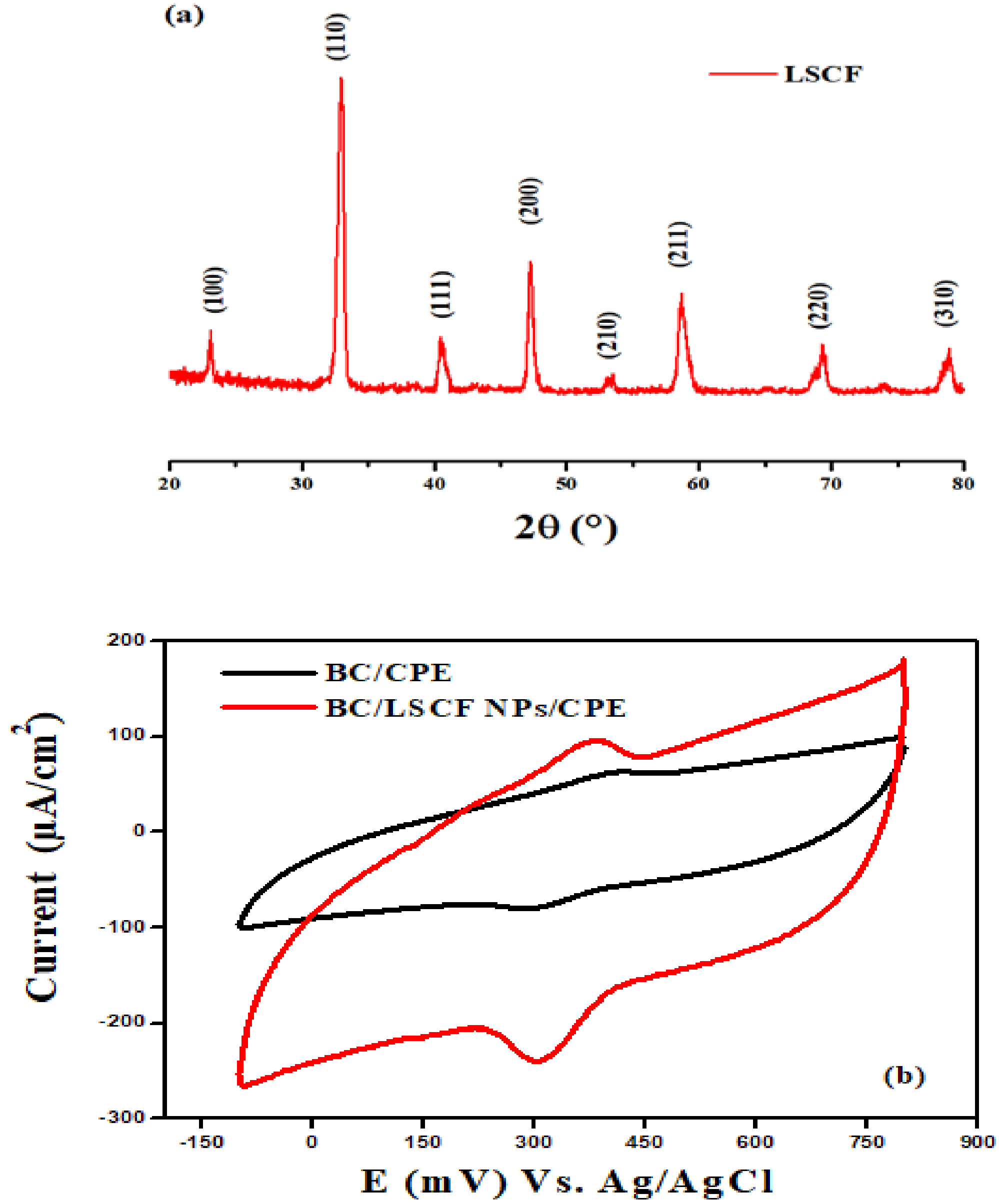


Figure 1. X-ray diffraction patterns recorded for $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ nano-sized particles synthesized by the citrate method, (b) CVs obtained for 3 mM $[Fe(CN)_6]^{4-}/[Fe(CN)_6]^{3-}$system mixture as electrolyte analyzed with BC+LSCF NPs and BC only two paste electrodes at 50 mV.s^{-1} scan rate in 0.1 mM phosphate buffer solution pH 7.4.

using SEM, all the obtained images are provided with a 1 µm scale bar. As depicted in Figure 2, the grains of LSCF nanomaterials exhibit homogeneity, primarily possessing a spheroid shape and uniform size distribution. Also, the micrographs reveal a significant presence of pores across various scales, enhancing their catalytic properties by increasing the specific surface area. This porous structure facilitates the diffusion and adsorption of drug molecules into both small and large pores of the modified CPE. The average grain size *d* of $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ synthesized nanoparticles was obtained from the histograms at 20x magnification, with the smallest values of 65.05 nm.

3.3 Ferro-cyanide test

Before any electrochemical detection study, it's of big importance to check out the kinetic process of the prepared CPE towards the ferrocyanide Red/Ox couple $[Fe(CN)_6]^{4-}/[Fe(CN)_6]^{3-}$ with 3 mM concentration in 0.1 mM PBS pH 7.0 [29, 30]. For this test, two pastes were prepared: one

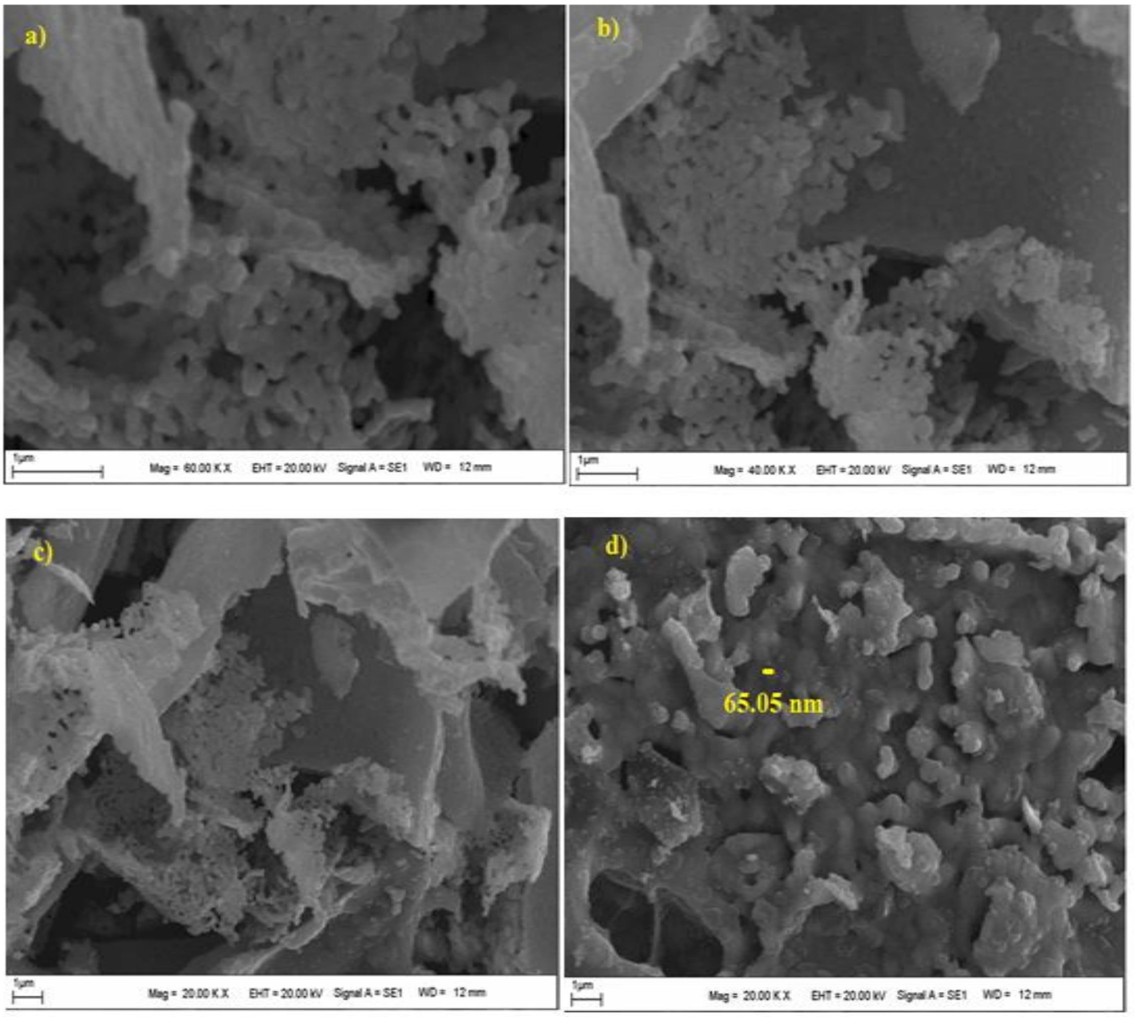


Figure 2. SEM surface images of $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$ nanomaterials at different magnifications (a) 60, (b) 40, (c) and (d) 20 (scale bar=1 µm).

paste composed of BC and ethylene glycol only, and the second paste consisted of BC and LSCF NPs grouped with ethylene glycol. Each paste was filled into a clean capillary glass tube and attached with a Pt wire for electrical contact. After that, the two pastes were studied as working electrodes for detecting the ferrocyanide system using the CV technique at 50 mV.s^{-1} scan rate. The comparative cyclic voltammograms of the two pastes are represented in Figure 1 (b). It was noted that the anodic electro-oxidation peak potentials (E_a) at the BC/CPE and the BC+CLFN NPs modified CPE were 450.068 mV (vs. Ag/AgCl) and 353.56 mV (vs. Ag/AgCl) respectively. Similarly, the cathodic electro-reduction potentials (E_c) were 300.068 mV and 313.27 mV, with the following potential differences (ΔE_P) of 150 mV/Ag/AgCl and 40.29 mV/Ag/AgCl, respectively. The observed low ΔE_P of BC+CLFN NPs modified CPE indicates the highest and fastest electron transfer between the BC+CLFN NPs/CPE surface area and ferro-cyanide couple. It is evident that electrodes modified with LSCF nanoparticles are more efficient and exhibit a superior electrocatalytic effect for both electron and mass transfer compared to those composed of BC only, and characterized with significantly higher current peaks, low potential values, and prominent peaks.

3.4 Electrochemical behavior of LSCF/BC/CPE modified electrode for PCM detection

3.4.1. PCM behavior with cyclic voltammetry

The effect of scan rate variation for the electro-catalytic mechanism of PCM drug and its stability towards our prepared CPE was investigated by varying the scan rates from (10 mV.s^{-1} to 400 mV.s^{-1}) with 100 µM of PCM concentration in 0.1 mM PBS at pH 7.0. It was noted that, with increasing the value of the scan rate, there was a notable proportional linear increase in the peak current I_P. Figure 3 (a) indicates that the oxidation and reduction peaks of the reversible system paracetamol were well controlled with a stable diffusion of PCM molecules towards the LSCF/BC/CPE surface area with a perfect correlation regression of 0.9984. From the cyclic voltammetric plots shown in Figure 3 (b), we note a reversible system of PCM drug at LSCF/BC/CPE modified sensor according to reaction (1) below. It is observed that increasing PCM concentration, results in a proportional increment in peak current with a fixed potential of 435 mV/Ag/AgCl approximately, this leads to the establishment of two linear regression equations: a) $I_1 = -18\ C + 44.20$, $R^2 = 0.902$ for the high concentrations of PCM, and b) $I_2 = -464.51\ C - 839.47$, $R^2 = 0.9923$ for low concentrations of PCM, with low detection and quantification limits of LOD = 0.38 µM and LOQ = 1.14 µM,

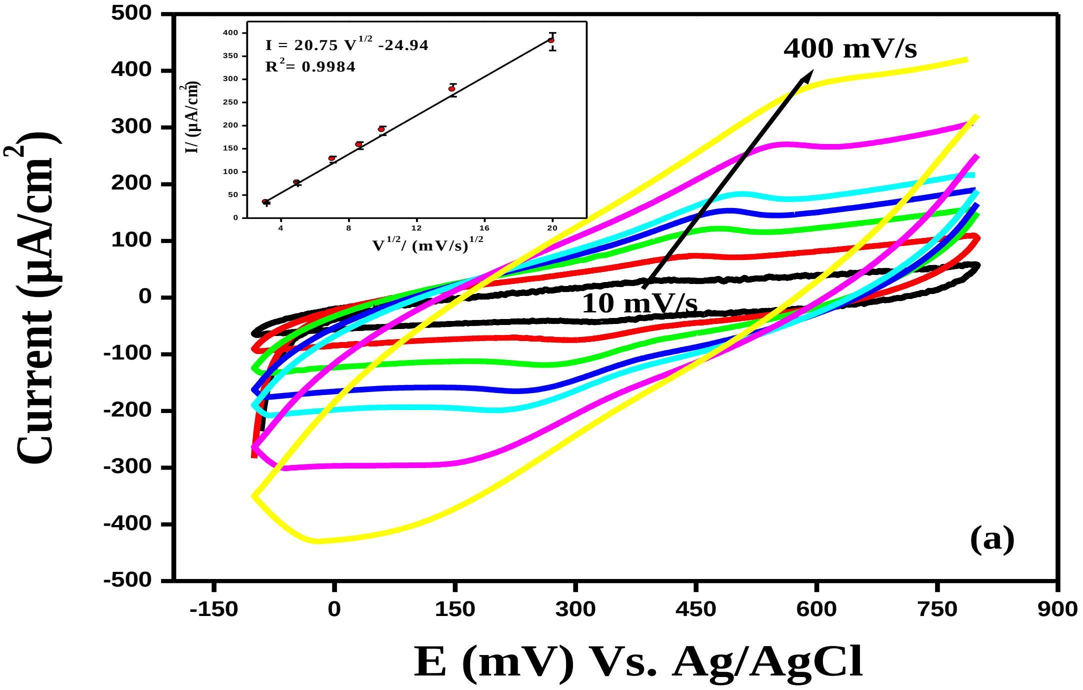
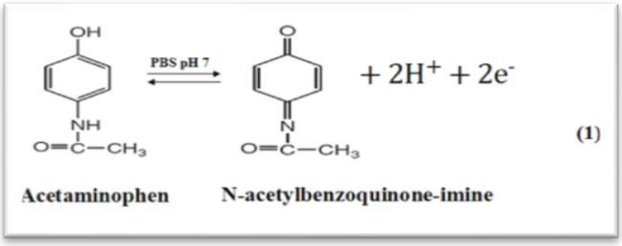


Figure 3. Scan rate variation from 10, 25, 50, 75, 100, 200 to 400 mV.s^{-1} of 100 µM PCM at (a) LSCF/BC/CPE, (b) Cyclic voltammograms plots for varied concentrations of PCM solutions (3 µM, 40, 80, 100, 120, 140, 160 to 180 µM), at 25 mV.s^{-1} scan rate in 0.1 mM PBS pH 7.4.

respectively, and high sensitivity of S = 464.51 µA.µM^{-1}.cm^{-2}. According to the reaction number (1), the oxidation mechanism of paracetamol in PBS pH 7.0 is a process of two electrons and two protons transfer [26]. As a result, the working electrode shows very high currents, well-pulsed, and prominent peaks, demonstrating its high sensitivity and selectivity towards paracetamol drug using the CV technique.

The mechanism of LSCF/BC/CPE towards PCM detection is as follows [21]:



Scheme 2. Suggested oxidation mechanisms for paracetamol drug.

The LOD was calculated using the following equation:

$$\mathrm{LOD} = 3 \times \frac{SD}{S} \qquad (1)$$

Where *SD* is the standard deviation of the blank and *S* is the slope or the sensitivity of the first linear range.

3.4.2. PCM determination with differential pulse voltammetry

The behavior of PCM at LSCF/BC/CPE was investigated using the DPV technique [30] in 0.1 mM PBS pH 7.0 with a wide linear range of 0.1 µM to 180 µM. For DPV measurement represented in Figure 4 (a), the electro-oxidation potential of PCM was approximately noted at +450mV/Ag/AgCl. Notably, well-defined, single, and prominent pulsed peaks were observed, also with increasing PCM concentration, the peak current exhibits a direct increment, indicating a proportional relationship between the current and diffused quantities of drug molecules, with the extracted regression equation from Figure 4 (b): I = 0.75 C-0.835, R^2 = 0.9812 with a very low detection and quantification limits of 0.036 µM and 0.11 µM and a high sensitivity of 75 µA.µM^{-1}.cm^{-2} respectively. In conclusion, DPV is the best electrochemical method for PCM monitoring because it is characterized by high sensitivity and selectivity, able to detect and follow very low concentration values until 36 nM which could not be achieved using the CV technique.

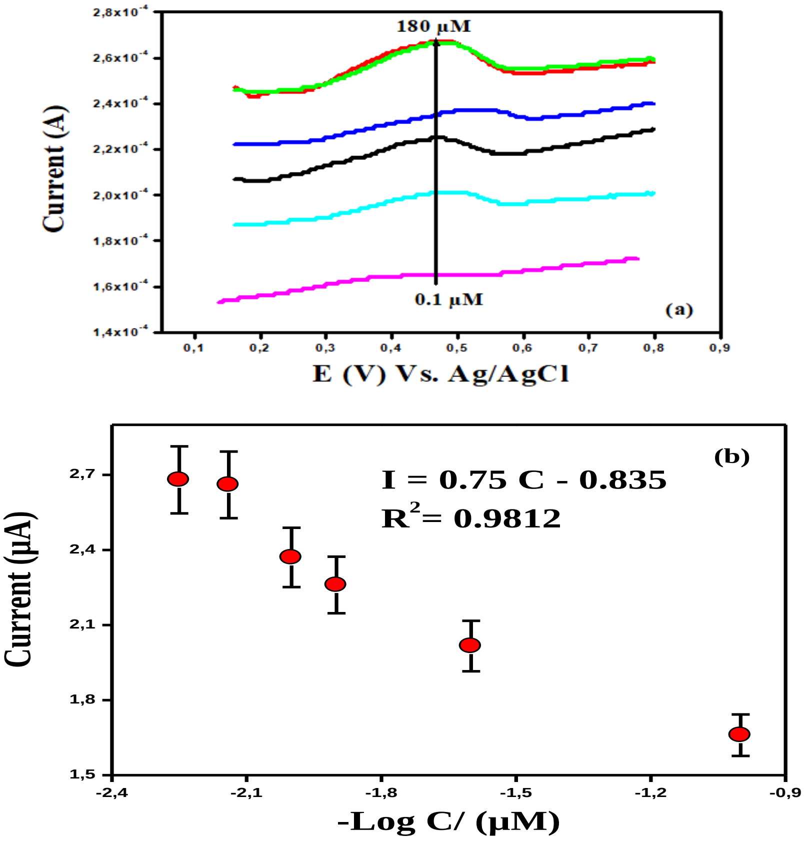


Figure 4. Differential pulse voltammetric plots for several concentrations of paracetamol (0.1 µM, 40, 80, 120, 160 to 180 µM), varied at LSCF NPs/BC/CPE with 50 mV pulse size, sample period of 0.2 s, pulse time of 0.1 s, and a step potential of 2.0 mV in 0.1 mM PBS pH 7.4.

3.4.3. PCM behavior with electrochemical impedance spectroscopy

The performance of LSCF nanoparticles onto the CPE towards the study of electron and ion transfer between electrolyte and electrode active surface area was investigated using EIS assay [29, 30]. Nyquist plots obtained are processed with electrochemical Zfit analysis by the EC-Lab program and represented in Figure 5. From the Nyquist plots shown in Figure 5 (a), concerned with the maximal concentration of PCM drug studied in the frequency interval of 10^5 to 10^{-2} Hz, we can observe three principal regions:

a) The primary response of electrolyte resistance (R_1) is observed at frequency levels higher than 10^5 Hz.

b) Between 10^5 to 10^{-1} Hz, a semi-circle of charge transfer (R_2) phenomenon occurs between electrode/electrolyte at these frequencies.

c) At frequency values under 10^{-1} Hz, a straight line is observable related to the adsorption and diffusion phenomenon of PCM species towards our working electrode surface area (R_3).

Figure 5 (b), illustrates all the Nyquist plots drawn between 10^5 to 10^{-1} Hz frequency domains, where the main mass and charge transfer phenomena characterizing the modified prepared electrode were subtracted. The resistances (R) and capacities (CPE) obtained are presented in Table 2. It's found that, with increasing the concentration of PCM drug, the charge transfer resistance R_2 increases directly, which means that the charge transfer resistance R_{ct} is directly proportional to PCM concentrations, which can be explained by the ease of ions mobility and high electronic exchange when the adsorbed concentration is high. Furthermore, the electrolyte resistances R_1 also exhibit proportional increment with raising the concentration levels of PCM drug.

Table 2. Different values of resistances and capacities extracted from the Nyquist plots at 10^5 to 10^{-1} Hz frequency domains and their corresponding fits using electrochemical Zfit analysis by EC-Lab program for different concentrations of paracetamol (3 µM to 180 µM) at LSCF material surface area.

Concentration (µM)	R_1 (Ω)	R_2 (Ω)	CPE_1 (F. s^{-1}).10^{-3}	CPE_2 (F. s^{-1}).10^{-3}
3	88.93	802.0	0.182	0.666
40	235.6	923.0	0.241	1.457
80	265.88	1162	0.547	3.174
120	700.2	1194	2.214	4.865
180	4845	1202	2.833	5.243

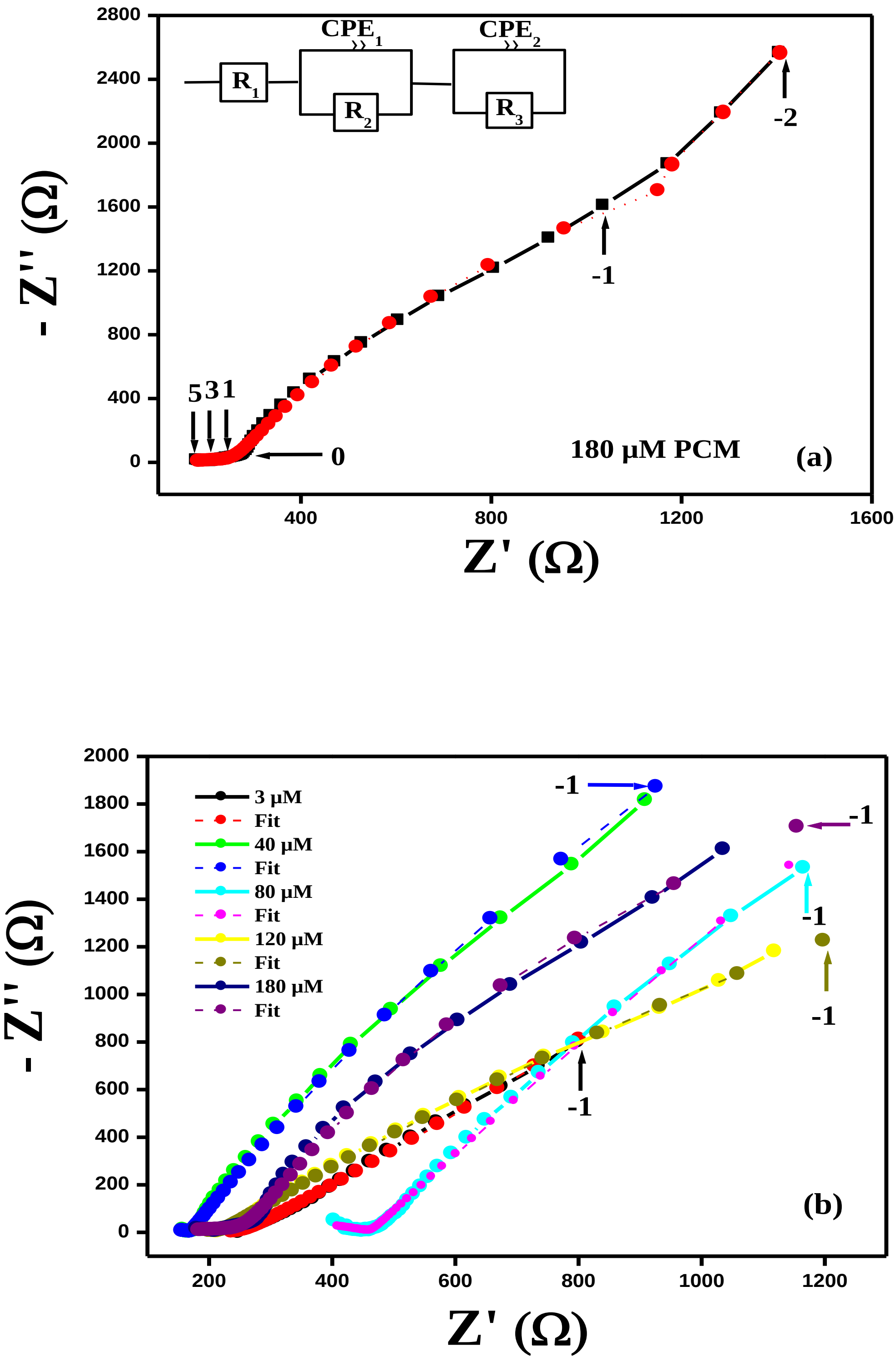


Figure 5. Nyquist plots for PCM drug at its maximal concentrations 180 µM, (a) at 10^5 to 10^{-2} Hz frequency domains, (b) several plots display the entire concentration range studied in CV technique with their corresponding fits at 10^5 to 10^{-1} Hz frequency domains.

3.5 Effect of pH on the electro-oxidation of PCM drug

The pH of the electrolyte is a crucial parameter for studying the best mechanism of the prepared electrode toward the PCM analyte [42]. To select the best electrolyte pH for paracetamol monitoring, the effect of pH solution on the anodic peak current of PCM at LSCF/BC/CPE from pH 2.0 to pH 12.0 was investigated. The voltametric plots of the peak current vs. pH represented in Figure 6 (a), show that the peak current responses increased at pH 2.0–6.0 with a first linear regression of $I_1 = 13.12 \text{ pH} + 46.56$, $R^2 = 0.9904$ with a good slope of 13.12 $\mu A.pH^{-1}$, then reaching the highest level at pH 7.4 resulting a well-shaped, predominant and the lower potential peak at (+399 mV/Ag/AgCl), then decreasing from pH 7.4 to 12.0 with the second linear regression of $I_2 = - 20.032 \text{ pH} + 372.85$, $R^2 = 0.963$ with excellent slope of 20.032 $\mu A.pH^{-1}$, herein the values of potentials change in a different way between (399 mV/SCE to 483 mV/SCE). The obtained results show that the estimated proton and electron exchange is low in both acidic and basic media, while the neutral environment (pH 7.4) offers the best appropriate proton media for electrocatalytic oxidation PCM detection. For this reason, all the experiments on paracetamol monitoring were carried out in PBS at pH 7.4.

3.6 Electrochemical performance of LSCF sensor in the real pharmaceutical sample

The performance of the modified $La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$NPs/BC/CPE sensor was checked using a real sample [43, 44], including pharmaceutical tablets containing paracetamol as the active ingredient and other components, the sample was purchased from PHYSIOPHARM laboratories. The pharmaceutical sample was dissolved in 100 mL PBS pH 7.0(10 µM) at a prepared concentration of 100 µM and analyzed using the developed sensor via CV technique. The scan rates were varied between 10 to 200 $mV.s^{-1}$. Based on the voltammograms shown in Figure 7 (a), it's clear to see that PCM as a real sample exhibited a reversible system as its active ingredient at (+376.55 mV). The diffusion of PCM drug is directly proportional to the increment of scanning rates, as confirmed by the corresponding linear equations: $I_P = -27.39 V^{1/2} + 24.73$, $R^2 = 0.9972$. The diffusion of the pharmaceutical product molecules towards the surface area of the working electrode is well controlled, exhibiting excellent correlation ($R^2 \approx 1$). Based on the voltammograms depicted in Figure 7 (b), comparing the behavior of paracetamol as an active ingredient and as a pharmaceutical tablet at the same concentration of 100 µM, no difference is observed for PCM mechanism; with presenting the same response with a

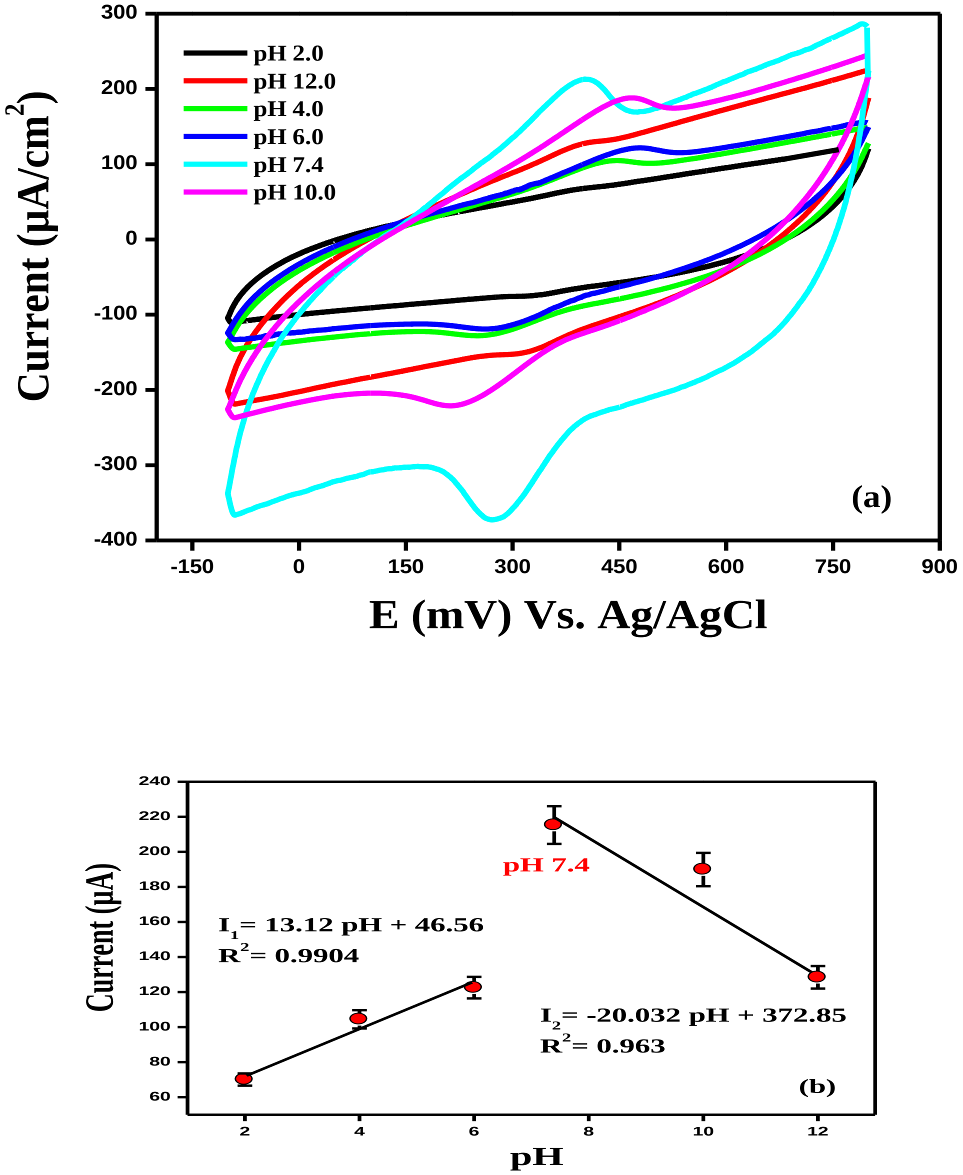


Figure 6. Cyclic voltammetric plots for several solutions of 100 µM PCM with different pH values (**pH 2.0** to **pH 12.0**) in 0.1 mM PBS.

reversible system, with only some difference in peak potentials (ΔE_{AI} = 81.15 mV ΔE_{Tab} = 145.8 mV). Additionally, PCM as an active ingredient exhibits higher current peaks and lower potential compared to PCM tablets, indicating superior electronic and mass transfer efficiency. The results obtained demonstrated high precision, with favorable recovery percentages of 92.24%, and 94.56% for PCM in PBS and as tablets, respectively. These percentages were calculated from equation number (2), with good relative standard deviations of 5.24% and 3.26%. In conclusion, the performance of the fabricated sensor towards PCM detection in real samples is comparable to its performance with its active ingredient. In addition, these results demonstrate high sensitivity and selectivity, reproducible, reliable precise and the technique is faithful and could be a good alternative for quality controlling of PCM drugs for health and environment preservation.

By comparing our prepared modified LSCF/BC/CPE after calculating its detection and quantification limits with previously developed electrodes (Table 4), it was found that our newly developed electrode characterized by: the best-widened concentration range for PCM sensing that can reach even to 36 nM with DPV technique. The highest sensitivity and the lowest detection and quantification limits compared with the literature and our CPE can considered the best performer of previous works with CPE sensors.

Table 3. Determination of the recoveries and relative standard deviations of the prepared modified electrode LSCF NPs/BC/CPE in PBS and real pharmaceutical sample.

Sample	**Original [C] (µM)**	**Found [C] (µM)**	**Recovery[1] (%)**	**R.S.D[2] (%)**
PBS	100	102.24	92.24	5.24
Tablets	100	104.56	94.56	3.26

[1] **Recovery** $= \frac{\text{Found [C]} - \text{Diluted biofluids [C]}}{\text{Original [C]}} \times 100$ (2)

[2] **R.S.D** = Relative Standard Deviation

Diluted biofluids [C] =10 µM PBS

Table 4. Comparison of the detection and quantification limits of LSCF/BC/CPE modified electrode with other previously developed modified carbon paste electrodes.

Electrode	**LOD (µM)**	**LOQ (µM)**	**Linear range (µM)**	**Technique**	**Ref.**
$MnFe_2O_4$ and $CoFe_2O_4$ NPs/GPE	0.25/$MnFe_2O_4$ 0.30/$CoFe_2O_4$	0.825 0.99	3-200 3-160	DPV	[21]
Stevensite-Modified Carbon Paste Electrode (Stv-MCPE)	0.2	0.6	0.6-100	CV, DPV	[22]
ZrO_2 NPs / Modified CPE	0.68	2.244	10-60	CV, DPV	[23]
Ionic Liquid Crystal (ILC)/CPE	2.8	9.24	0-120	DPV	[24]
La_2NiO_4 and Pr_2NiO_4 NPs/CPE	1.99/La_2NiO_4 2.04/Pr_2NiO_4	6.57 6.732	3-200	CV, SWV	[26]
Poly (L-leucine)/ Modified CPE	0.44	1.452	90-200	CV, DPV	[28]
LSCF/BC/CPE	**0.036**	**0.11**	**0.1-180**	**CV, DPV**	**This work**

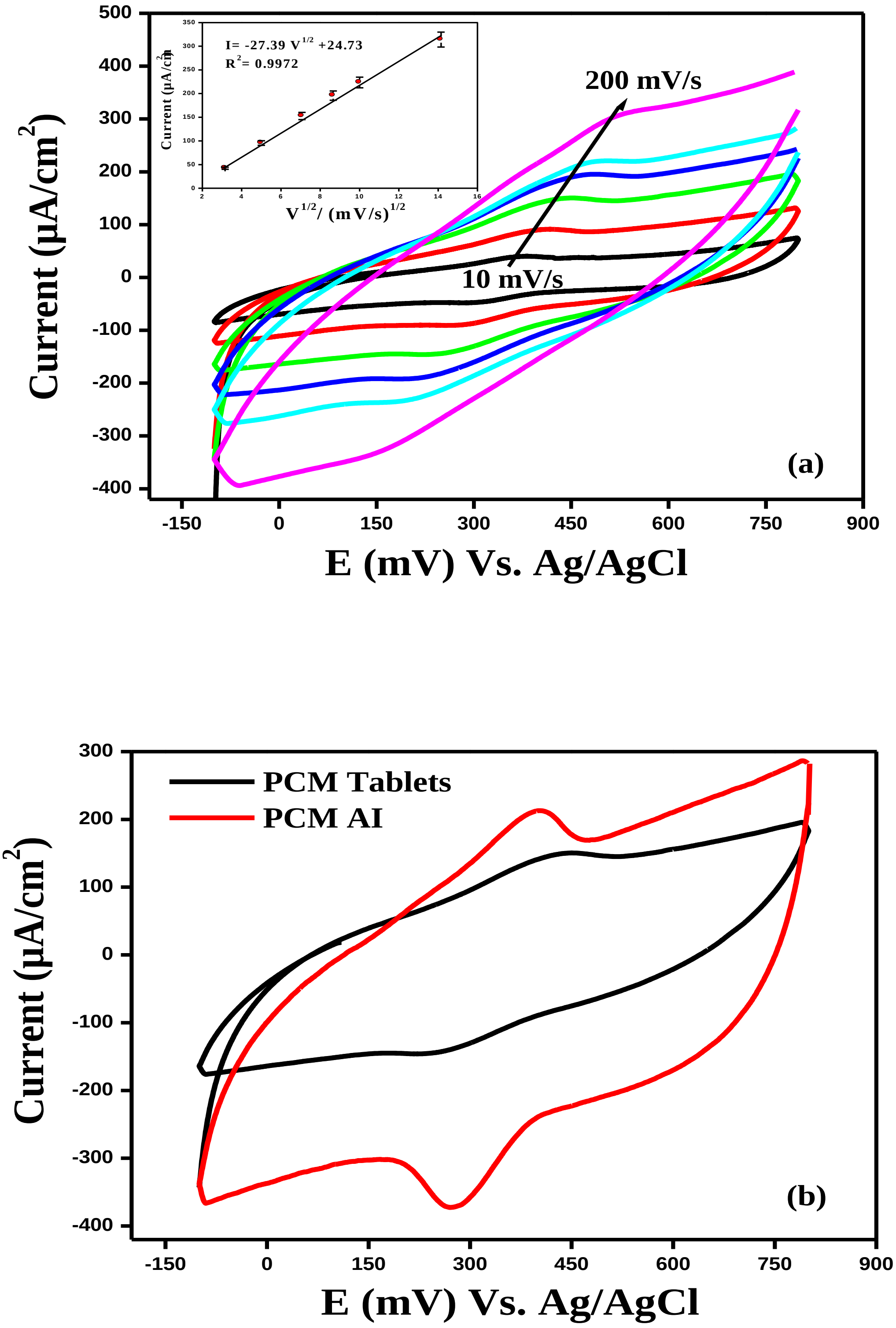


Figure 7. CV plots, (a) using LSCF/BC/CPE at varied scan rates from 10, 25, 50, 75, 100 to 200 mV.s^{-1} in the real sample of PCM drug (100 µM), (b) CV plots of PCM as active ingredient (AI) and as pharmaceutical tablets with 100 µM concentration, at 100 mV.s^{-1} scan rate in 10 µM PBS pH 7.

4 CONCLUSIONS

In conclusion, a novel, cost-effective, and highly efficient electrocatalyst ($La_{0.6}Sr_{0.4}Co_{0.8}Fe_{0.2}O_3$), modified with BC and integrated into a CPE, was successfully developed for simultaneous electrochemical sensing of paracetamol. The monitoring electrochemical techniques were CV, DPV, and EIS assay. The developed sensor demonstrated a broad linear detection range (0.1–180 µM) via DPV, ensuring high analytical reliability. This modified electrode was carried out for the precise quantification of PCM in PBS with low detection limits of 36 nM in DPV, and 380 nM in CV, respectively. The sensor's practical applicability was validated using a real pharmaceutical sample, yielding highly reproducible recovery rates of 92.24% (PBS) and 94.56% (tablet form), with relative standard deviations (RSDs) of 5.24% and 3.26%, respectively. The sensor exhibited high sensitivity, selectivity, and stability. Overall, the modified LSCF/BC/CPE sensor exhibited rapid, highly sensitive, and reproducible performance for PCM detection, making it a promising candidate for pharmaceutical quality control applications.

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6 AUTHOR CONTRIBUTIONS

Writing – original draft, Validation, Conceptualization, Methodology, Visualization: M.M.; Supervision: M.F.; Investigation, Writing – review-editing: M.F., E.K.S.

7 CONFLICT OF INTEREST

The authors declare no conflict of interest, and all co-authors have approved the final version of this manuscript.

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