

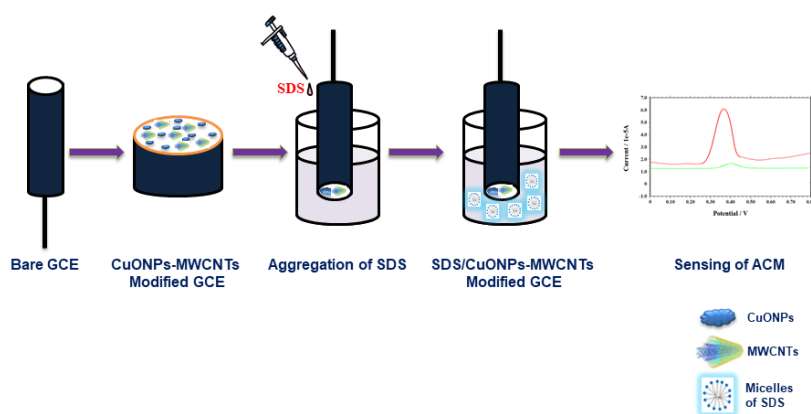
ARTICLE

Sensitive Voltammetric Detection of Acetaminophen on CuONPs-MWCNTs Modified Glassy Carbon Electrode with Enhancement Effect of Anionic Surfactant

Rajesh N. Hegde^{1*}  , P. Vishwanatha¹ , Sharanappa T. Nandibewoor² 

¹Department PG Studies and Research in Chemistry, Sri Dharmasthala Manjunatheshwara College, Ujire-574 240, Karnataka, India

²K L E Technological University, Hubballi-580 031, Karnataka, India



In the present work, a voltammetric method using differential pulse voltammetric technique was developed for the assessment of antipyretic and analgesic drug, acetaminophen. The CuO nanoparticles were prepared and characterized. A glassy carbon electrode (GCE) fabricated with the suspension of CuO nanoparticles (CuONPs) and multi-walled carbon nanotubes (MWCNTs) were used. The modified electrode showed improved

anodic peak current by introducing an anionic surfactant sodium dodecyl sulphate in phosphate buffer solution. The effect of the pH of the supporting electrolyte, the amount of nanoparticle suspension and the surfactant concentration was studied at a physiological pH of 7.4. Using differential pulse voltammetry, the fabricated electrode showed linear dynamic range from 9 to 160 nM of acetaminophen concentration. From the calibration plot, the computed detection limit was 5.06 nM and quantification limit was 16.88 nM. The developed method was tested for its reproducibility and assay during a day and intraday as well. The developed process was fruitfully applied to detect acetaminophen in pediatric oral suspensions administered to infants.

Keywords: voltammetry, acetaminophen, surfactant, nanoparticles, sensor

INTRODUCTION

Acetaminophen (ACM), is the most widely studied pharmacological and hepatotoxic drug used by billions of people globally as an antipyretic and analgesic therapeutic drug. It is believed to be safe when

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administered in lower doses and it relieves moderate to severe pain and is being used to treat fever. ACM administered to healthy adults is metabolized in the liver and excreted in the urine.¹ Of the administered dose, only about 1-4% is released as pure ACM and most is converted to conjugated forms such as paracetamol glucuronide; about 47-60% is released as paracetamol sulfate and about 25-35% is excreted from the human body. At higher dosage, ACM proved to be deadly for humans and also causes disturbance of heart and mind. The extended and too much use of ACM may lead to toxic metabolite amassing and this can cause failure of kidney and liver or even death. Therefore, it becomes very essential to develop an analytical technique to analyze ACM in various samples.

To date, there are many analytical methods used to analyze and quantify various drug molecules either in real samples or pharmaceutical samples. Among the methods developed, spectroscopic, chromatographic, titrimetric and electrochemical methods are widely used.²⁻⁷ Among all these methods, the electrochemical methods have been strongly developed in recent years because they are cost effective, reliable, require less time for analysis, very simple with good selectivity and high sensitivity. These methods also fall in sustainable analytical methods because of no or less solvent usage. The electrodes based on carbon materials are being employed widely in electrochemical analysis, since they have broad potential window, brilliant electrical conductivity, very little background current, more surface area for reaction, chemically and electrochemically inert, highly stable and very much cost effective.⁸⁻¹⁰ High sensitivity and excellent selectivity were achieved by employing modified electrodes using various types of modifiers, especially with the nano-dimensional materials, either carbon based nano-materials or metal based nano-materials or even nano-composites.^{11,12}

The surface active substances, i.e., the surfactants are playing vital role in the development of electrochemical sensors in recent years. Surfactants can enhance the electrochemical process which is occurring at the electrode there by excelling the sensitivity of the fabricated electrode via adsorption at interfaces or aggregation into supramolecular structure. In recent days, the surfactants were used to enhance the sensitivity of the methods.^{13,14} The SDS is also been used widely to improve the detection and quantification limits of the methods developed.^{15,16}

To date, ACM was one of the drug molecules which was extensively studied and detected using various modified electrodes with very low detection limits in different formulations. There was a report on paracetamol sensing using graphite flakes.¹⁷ MWCNTs decorated silver nanoparticles were used to sense ACM with good detection limit and recovery.¹⁸ There was an attempt to study electrochemical kinetics of ACM and its detection on a carbon paste electrode, even though this is economical, but it was bit difficult to produce same surface area using carbon paste electrode.¹⁹ Simultaneous detection of ACM and caffeine was reported using bare graphite electrode, but this lacks in sensitivity.²⁰ A polyglycine modified GCE was used to detect ACM in syrup with good sensitivity and selectivity.²¹ A screen printed carbon electrode was used successfully for the assessment of ACM, acetylsalicylic acid, caffeine simultaneously with good selectivity.²² An sensor for ACM detection was developed using guanine modified electro, but which is lacking in selectivity and sensitivity.²³ A nanomaterial-poly composite electrode was fabricated for ACM detection in biological fluids with excellent detection limit and sensitive.²⁴ There was an attempt to recover graphene oxide from Zn-C battery waste to construct a sensor for detection of ACM.²⁵ The recovery procedure was not so convincing and limit of detection reported was on higher side. ACM and ciprofloxacin were detected simultaneously on a sub-microparticle modified electrode with good linearity range.²⁶ There was an attempt to develop an organometallic complex encapsulated in nanozeolite electrode.²⁷ The modified electrode shown excellent electrocatalytic activity for the detection of ACM and ascorbic acid together with good linear range and detection limit. A pencil graphite electrode modified with polymer and gold nanoparticles was constructed.²⁸ They reported simultaneous assessment of ACM, propyphenazone, and caffeine with good linear range for ACM. A natural zeolite and graphene oxide were used to fabricate carbon paste electrode for the enhanced detection of ACM.²⁹ The DPV technique used to quantify ACM with excellent linearity range and limit of detection. The square wave voltammetric technique was used to detect ACM using 3D graphene platform.³⁰ Metal organic framework are now receiving great attention

because of their versatility. ACM was detected using NiCo-MOF with a fair detection limit.³¹ Eventhough, there are excellent reports for the detection of ACM, there is need to introduce new electrodes in the field of electro-analytical chemistry and to develop a better method for the sensing of ACM. Therefore, in this work, the CuONPs-MWCNTs modified electrode was fabricated and the signal of oxidation in PBS of physiological pH was significantly enhanced by introducing SDS into the solution. All the parameters were optimized using DPV and the developed method was fruitfully applied to detect ACM in syrups which were administered to infants.

MATERIALS AND METHOD

Chemicals

Multi Walled Carbon Nanotubes (MWCNTs; O.D. \times L of 7-15 nm \times 0.5-10 μ m), ACM, Triton X-100, cetyl trimethyl ammonium bromide (CTAB), sodium dodecyl sulphate (SDS), and $K_3Fe(CN)_6$ were purchased from Sigma-Aldrich. The other chemicals, methanol, NaH_2PO_4 , Na_2HPO_4 , and acetonitrile were purchased from Rankem Chemicals. To prepare the phosphate buffer solution (PBS), double distilled water was employed. The pH of PBS was varied from 5.4 to 8.0 by employing various volumes of dibasic and monobasic sodium phosphate stock solution. The stock solution of ACM was prepared in methanol. The pediatric oral suspensions produced by different companies and available locally were collected. Calpol (100 mg mL⁻¹) by Enzyme Pharmaceuticals, Gujarat; Akmol-25 (250 mg mL⁻¹) by Akiez Remedies, Varanasi; Dolopar (125 mg mL⁻¹) by Micro Labs Ltd and Wellpar (125 mg / 5 mL) by Wellona Pharma were purchased from local pharmacy. For stock solution preparation, exact volume was measured from syrup bottles and dissolved initially in methanol and diluted with distilled water. To get sufficient concentration to carryout analysis, required volume of PBS was used to dilute the above stock solution.

Instruments

Voltammetric measurements were carried out on a CH Instruments electrochemical analyzer 660E, attached with a conventional three-electrode cell. The three-electrode cell consisting of a bare glassy carbon electrode with a diameter of 2 mm (modified and unmodified) as working electrode, a Pt wire was used as the counter electrode and an Ag/AgCl (3 M KCl) as reference electrode, respectively. All the potentials recorded in this report were specified against the Ag/AgCl electrode. An alumina powder 0.05 μ m was used to polish the surface of working electrode and was cleaned ultrasonically. Then, to characterize the prepared CuO nanoparticles, scanning electron microscope with model specification of SEM XL 30 ESEM with EDAX was used.

Preparation and characterization of nanoparticles of CuO

The nanoparticles of CuO were synthesized as reported elsewhere.³² By mixing vigorously 0.5 M Na_2CO_3 solution and 0.5 M $CuSO_4$ solution at about 80 °C, the precursor was prepared. This results in basic copper sulphate precipitate, which was filtered immediately and washed to remove the ion traces with doubly distilled water. Then, it was filtered and mass was left for drying in air for 8 hours. The precursor was thermally decomposed in a muffle furnace for a period of 4 hours at 800 °C which results in the production of nanoparticles of CuO. Then, the SEM image of the prepared nanoparticles was recorded after calcinations and is as shown in Figure 1.

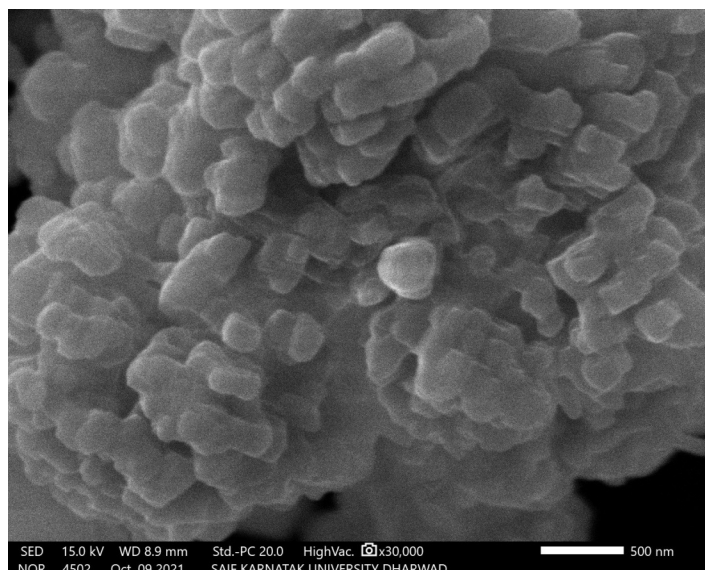


Figure 1. Scanning electron microscopic image of CuO nanoparticles.

Analytical procedure

By breaking up 2 mg each of MWCNTs and CuONPs in acetonitrile (10 mL), the CuONPs-MWCNTs stable suspension was prepared by ultrasonication. The working electrode was polished carefully with the slurry of 0.05 μm alumina powder using the polishing cloth, and then washed with methanol and water in an ultrasonic bath, respectively. Thus, cleaned working electrode was drop-coated with 5 μL of the black suspension of CuONPs- MWCNTs every time and dried in air.

The CuONPs-MWCNTs fabricated GCE was first activated in PBS of pH 7.4 by cyclic voltammetric measurements from 0.0 to 0.8 V until we get stable segments of cyclic voltammograms with a scan rate of 0.05 V s^{-1} for 5 cycles. After that, electrodes (all three) were transferred to second cell of PBS with pH 7.4, which contains accurate amounts of ACM and SDS. With an increment of 0.04 V, amplitude of 0.05 V, pulse width of 0.05 s, sample width of 0.0167 s and pulse period of 0.5 s, the differential pulse voltammogram was recorded between 0 and 0.8 V. All the experiments were performed at 25 $^{\circ}\text{C}$ in presence of atmospheric oxygen.

RESULTS AND DISCUSSION

Response of modified electrode with potassium ferricyanide

A 1.0 mM solution of $\text{K}_3\text{Fe}(\text{CN})_6$ in 0.1 M KCl was used to record CVs at CuONPs-MWCNT modified GCE at various scan rates. For the reversible electrode process, the Randles-Sevcik equation (Equation 1) was used to calculate effective surface area of unmodified and modified electrode.

$$I_p = (2.69 \times 10^5) n^{3/2} A D^{1/2} C_0 v^{1/2} \quad \text{Equation 1}$$

where I_p is the anodic or cathodic peak current, n is the number of electrons involved, A is the electrode surface area, D is diffusion coefficient, v is the scan rate, and C_0 is the concentration of $\text{K}_3\text{Fe}(\text{CN})_6$

For 0.1 M KCl electrolyte with 1.0 mM solution of $\text{K}_3\text{Fe}(\text{CN})_6$, the n and D values are 1 and $7.6 \times 10^{-6} \text{ cm}^2 \text{ s}^{-1}$. By slope of the plot of $I_p v/s v^{1/2}$, the active surface areas obtained are 0.1462 cm^2 for modified GCE and 0.03925 cm^2 for bare GCE. From these values, it was concluded that active surface area has become significantly increased after fabrication. Therefore, it was concluded that modification of electrode showed electrocatalytic nature.

Response of ACM

The DPV was recorded for 100 nM ACM with 10 μ M of SDS and without SDS on CuONPs-MWCNTs/GCE. Without SDS, the oxidation peak at about 0.41 V was slightly weaker (Figure 2 (a)) compared to the peak in the presence of SDS at about 0.38 V, with significant enhancement in peak current and negative shift in peak potential (Figure 2(b)). It was well known that SDS can form micelles by self-assembly, which contains hydrophobic tail forming the core and hydrophilic head facing the outer surface. The introduction of SDS into the solution effectively reduces the interface between the electrode and ACM. This reduction in the interface is clear from the enhancement in the peak current as indicated in Figure 2 (b). The added SDS is facilitating the electro-oxidation process there by allowing the analyte to reach the electrode surface and take part in the redox reaction more conveniently by reducing the interaction between the electrode surface and the ACM.^{33,34}

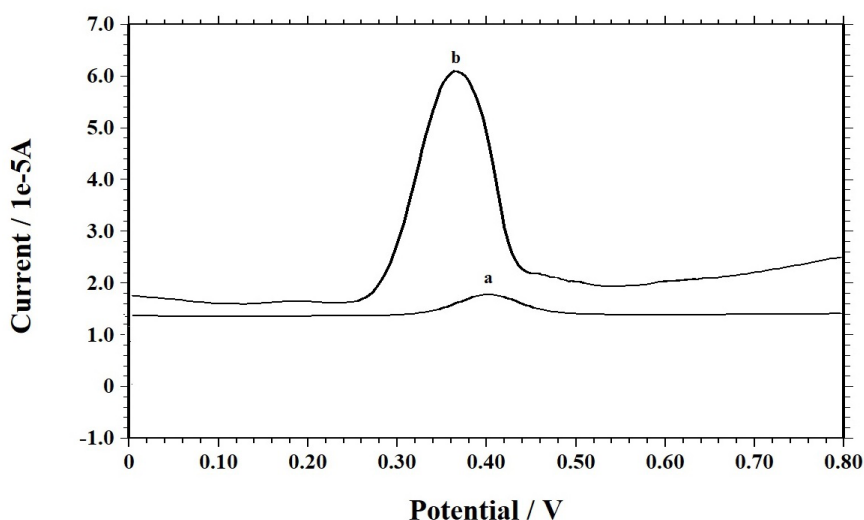


Figure 2. Differential pulse voltammogram of 100 nM ACM at pH 7.4 in 0.1 M PBS on CuONPs-MWCNTs modified GCE (b) with 10 μ M of SDS and (a) without SDS.

Effect of quantity of CuONPs-MWCNTs suspension and pH

The effect of the amount of CuONPs-MWCNTs suspension on the anodic peak was investigated. Highest oxidation peak current was obtained when 15 μ L of suspension was employed for drop coating. The peak current increased significantly with increasing the amount of the suspension till 15 μ L and afterwards, peak current decreased gradually and remain almost constant for higher concentrations of the suspension (Figure 3). This was owing to the fact that at higher quantity, the film is thicker and this results in reduced conductivity, which results in decreased oxidation current. Therefore, 15 μ L of suspension was utilized for further studies. The effect of pH was investigated from 8.0 to 5.8 using PBS, since pH of the supporting electrolyte plays key role in the reactions which take place at the electrode. The investigation indicated that, the oxidation potential was shifted to lesser values with increase in pH of the reaction medium. There was no significant variation in peak current, but physiological pH was employed for further studies.

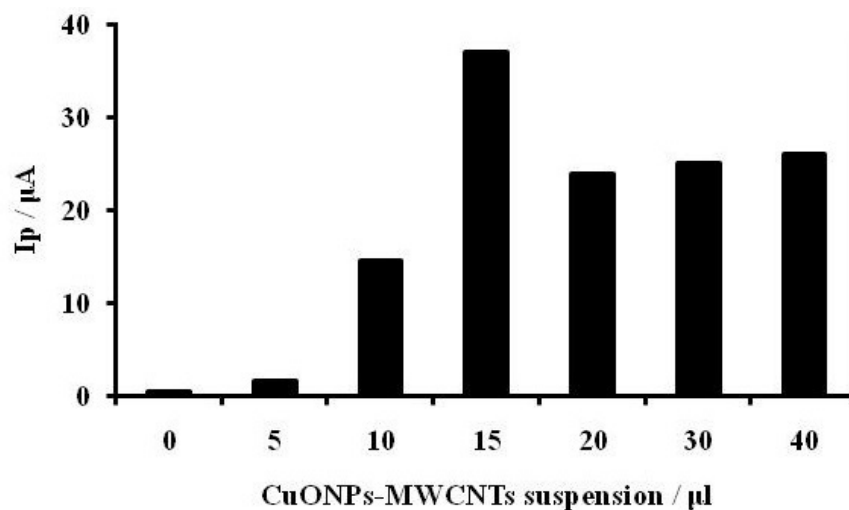


Figure 3. Graph of variation of volume of CuONPs-MWCNTs suspension against peak current.

Effect of surfactants

The influence of different types of surfactants has been tested for this title reaction. It was found that, in presence of neutral surfactant Triton X-100 there was no change in peak current and peak potential. However, in the presence of the cationic surfactant CTAB, the oxidation peak was poorly defined. Even though, an anodic peak was present in the company of all surfactants. However, the added SDS was effectively promoting the electro-oxidation of ACM at the electrode. The effect of concentration of SDS on oxidation reaction was examined. The peak current increased sharply up to 10 μM of SDS (Figure 4).

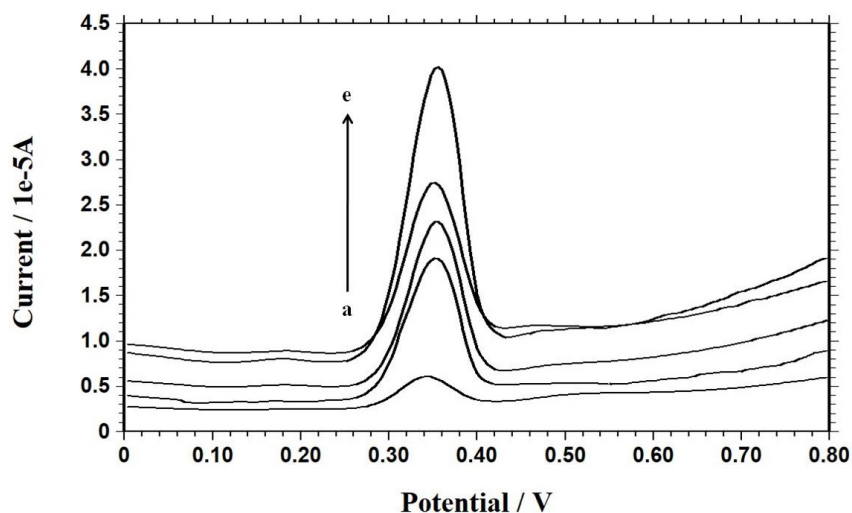


Figure 4. Differential pulse voltammograms of 100 nM ACM on CuONPs-MWCNTs modified GCE with (a) 0.0, (b) 2.5, (c) 5.0, (d) 7.5 and (e) 10 μM of SDS at pH 7.4 in PBS.

Afterwards, the peak current decreased gradually as shown in Figure 5. This may be due to the formation of thick aggregates of SDS at the electrode, which are blocking the surface for the reaction. Hence, 10 μM of SDS was employed for the further studies.

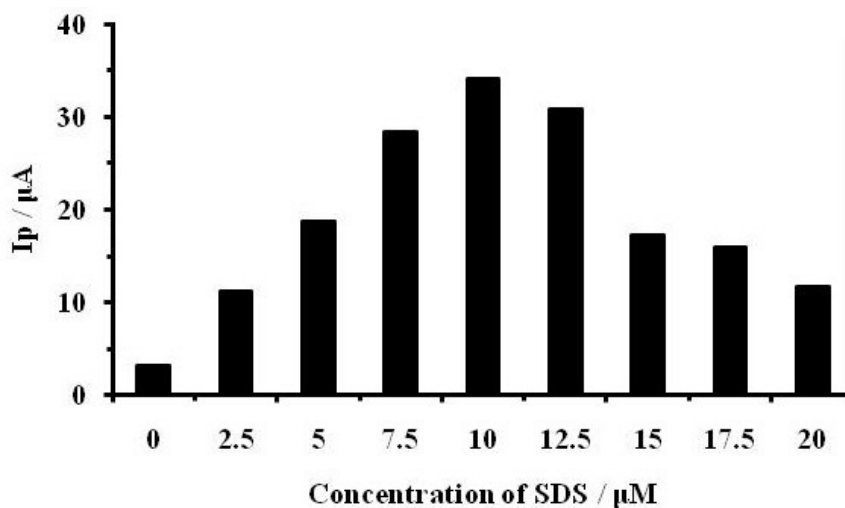


Figure 5. The plot of variation of peak current with concentration of SDS.

Calibration curve

To develop a voltammetric method for the estimation of ACM, DPV was used since the peaks are sharper and well defined using pulse techniques with lower background current. Using PBS as supporting electrolyte at physiological pH, voltammograms were recorded with increasing amount of ACM. The oxidation peak current rose linearly from 9.0 to 160 nM of ACM as shown in Figure 6. The calibration plot was constructed (Inset Figure 6.) which yields the equation $I_p = 0.22 C + 3.58$; $R^2 = 0.996$ (C is in nM). It was also observed that, variation from linearity for the higher quantity of ACM, due to the adsorption of analyte or its product after electro-oxidation on the surface of electrode. Using the equations, 3s/m and 10s/m, the detection limit and quantification limits were computed. The obtained detection limit and quantification limit are 5.06 nM and 16.88 nM respectively. These acquired outcomes were matched up with previously reported values and were tabulated in Table I.

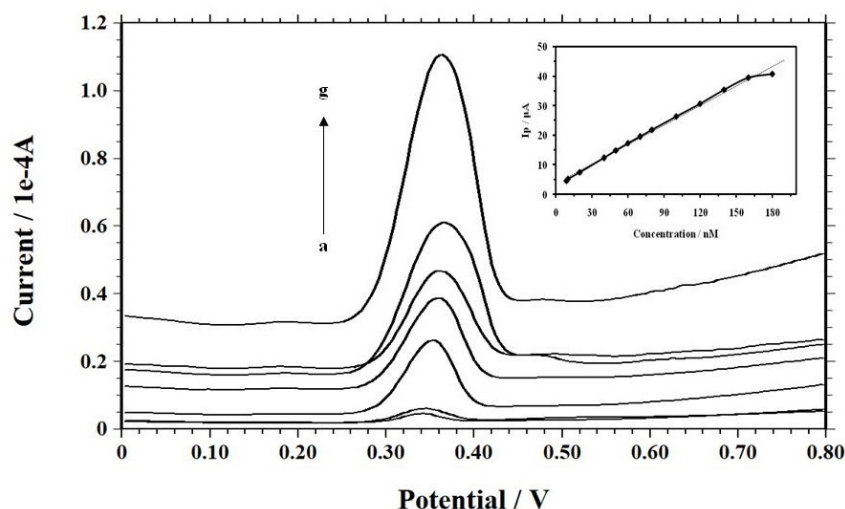


Figure 6. Differential pulse voltammograms with increasing quantities of ACM from (a) 9, (b) 20, (c) 40, (d) 60, (e) 80, (f) 120, and (g) 160 nM at SDS/ CuONPs-MWCNTs modified GCE in PBS. Inset: Plot of peak current Vs concentration of ACM.

Table I. Comparison of analytical parameters at various electrodes

Electrode	Method	LDR (μM)	LOD (μM)	Ref.
ePAD	DPV	1-60	0.20	17
AgNPs@HOOC-MWCNT@SPCE	SWV	0.5-1000	0.24	18
Stv-CPE	DPV	0.6-100	0.20	19
BGE	DPV	5-150	0.20	20
Polyglycine-GCE	DPV	0.5-75	0.03	21
SPCE	SWV	—	1.2	22
Guanine-GCE	DPV	0.005-10	0.90	23
MWCNT/GO/Poly(Thr)/GCE	DPV	3-140	0.16	24
ERGO-GCE	DPV	—	0.14	25
C-HAP-GCE	DPV	0.01-1310	0.14	26
NiCoSalenA/CPE	DPV	1.71-32.5	0.51	27
AuNPs/P(L-cyst)/PGE	DPV	0.023-90	—	28
GO/NiZ/CPE	DPV	0.026-0.78	0.007	29
3D/LSG	SWV	0.005-1	—	30
NiCo-MOF/CCE	DPV	5.0-400	1.0	31
SDS/CuONPs-MWCNTs/GCE	DPV	0.009-0.16	0.005	This work

ePAD - Electrochemical paper based analytical device; AgNPs – Silver nanoparticles; MWCNT – Multi walled carbon nanotubes; SPCE – Screen printed carbon electrode; Stv-Stevensite; CPE- Carbon paste electrode; BGE – Bare graphite electrode; GCE – Glassy carbon electrode; GO – Graphene oxide; ERGO – Electrochemically reduced graphene oxide; HAP – Hydroxyapatite; NiCoSalenA - Nickel-Cobalt Salen nanozeolite; PGE – Pencil graphite electrode; NiZ – Nickel ion zeolite; LSG – Laser scribed graphene; CCE- Carbon cloth electrode ; SDS – Sodium dodecyl sulphate; LDR – Linear dynamic range; LOD – Limit of detection; DPV – Differential pulse voltammetry; SWV – Square wave voltammetry.

Reproducibility study

To study the reproducibility of the fabricated electrode, voltammograms were recorded with 100 nM ACM at the fabricated electrode, which was re-modified each time for every few hours during a day. The relative standard deviation (RSD) of 2.02% was found for anodic current with 15 measurements and the modified electrode can be used thrice within 5% error. The reproducibility of results between days was analogous to that of within a day at constant temperature. However, the oxidation product was strongly adsorbing on to the electrode and hence the electrode has to be fabricated all over again after each run.

Intra-day and Inter-day assay

To substantiate the accuracy and precision of the above developed process, the assay of ACM was carried out during inter-day and intra-day. This was carried out at various amounts of ACM, i.e., at 10, 80 and 150 nM. Using DPV, voltammograms were recorded one time during a day ($n = 6$) for five successive days for the inter-day analysis and under alike state at the identical amounts of ACM ($n = 6$) for five times during a day to compute assay in a day.

During a day assay, the accuracy values obtained were $\pm 1.20\%$, $\pm 0.43\%$, and $\pm 0.75\%$ for low, medium and high concentrations levels with recovery values of 101.20%, 99.56% and 100.75%, respectively (Table II). For inter-day assay, the accuracy values of $\pm 0.60\%$, $\pm 0.53\%$ and $\pm 0.58\%$ were got with recovery values of 99.40%, 100.53% and 99.42% for low, medium and high quantity of ACM, respectively. The average precision values obtained were in the range of 4.67% to 10.24% (Table II). The precision and accuracy values computed were within $\pm 15\%$, and are hence within tolerable limits.³⁵

Table II. Statistics obtained for ACM assay during a day and inter-day

Quantity (nM)	Estimated quantity (nM)	Recovery (%)	Accuracy (%)	Precision (%RSD)
Intra-day				
10	10.12 \pm 0.42	101.20	\pm 1.20	6.13
80	79.65 \pm 0.64	99.56	\pm 0.43	9.75
150	151.1 \pm .32	100.7	\pm 0.75	5.32
Inter-day				
10	9.94 \pm 0.21	99.40	\pm 0.60	10.24
80	80.43 \pm 0.17	100.5	\pm 0.53	4.67
150	149.1 \pm 0.35	99.42	\pm 0.58	8.74

Assessment of ACM in oral suspensions

By following the identical conditions described above, the assessment of the analyte was carried out. The stock solution was diluted with doubly distilled water so that ACM concentration fall in LDR and introduced into the cell containing accurate quantities of PBS of pH 7.4 and SDS. DPV measurements were recorded and standard addition method was used to compute the concentration of ACM in syrup samples as shown in Figure 7. The computed results were as shown in Table III. It was found that, ACM concentrations obtained by the present method were matching with the labeled claim.

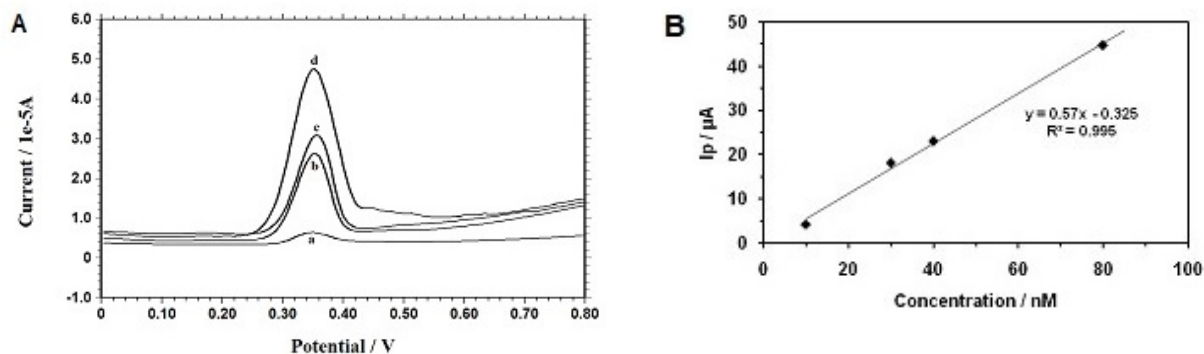


Figure 7. (A) Differential pulse voltammograms for (a) 10 nM ACM, (b) 30, (c) 40, and (d) 80 nM ACM in Calpol syrup at SDS/ CuONPs-MWCNTs modified GCE in PBS; (B) Calibration graph for standard addition method.

Table III. Results computed for ACM assay in syrup samples

	Calpol ^a	Akmol-25 ^a	Dolopar ^a	Wellpar ^a
Labeled claim (mg)	100	250	125	125
Amount found (mg) ^b	98.94	249.8	123.8	124.2
Added (nM)	80	80	80	80
Found (nM)	79.02	79.32	78.73	78.82
Recovered (%) ^b	98.77	99.15	98.41	98.53

^aName of syrups^bMean of five experiments

CONCLUSIONS

In the present effort, a glassy carbon electrode was fabricated with the suspension of CuO nanoparticles and multi walled carbon nanotubes for electro-oxidation and detection of ACM with the aid of anionic surfactant sodium dodecyl sulphate in PBS. This fabrication introduced a new electrode in the field of electro-analytical chemistry. The fabricated GCE proved the electro-catalytic nature for electro-oxidation of ACM, as indicated in anodic peak current enhancement. This modified electrode showed higher sensitivity, lower detection limit and good recovery values at pH 7.4. The ACM present in various syrup samples were detected using the developed method productively. More efforts are needed to fabricate novel electrodes to detect ACM in real time with good stability.

Conflicts of interest

Authors declare no conflicts of interest.

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REFERENCES

- (1) van der Marel, C. D.; Anderson, B. J.; van Lingen, R. A. Paracetamol and metabolite pharmacokinetics in infants. *Eur. J. Clin. Pharmacol.* **2003**, *59*, 243-251. <https://doi.org/10.1007/s00228-003-0608-0>
- (2) Siddiqui, M. R.; Othman, Z. A.; Rahman, N. Analytical techniques in pharmaceutical analysis: A review. *Arab. J. Chem.* **2017**, *10*, S1409-S1421. <https://doi.org/10.1016/j.arabjc.2013.04.016>
- (3) Sharma, S.; Singh, N.; Ankalgi, A. D. Modern trends in analytical techniques for method development and validation of pharmaceuticals: A Review. *J. Drug Deliv. Ther.* **2021**, *11*, 121-130. <https://doi.org/10.22270/jddt.v11i1-s.4515>
- (4) Chavan, A.; Gandhimathi, R. Modern analytical tools for the determination of the active pharmaceutical ingredients: a review. *Int. J. Pharm. Sci. Res.* **2022**, *13*, 61-69. [http://dx.doi.org/10.13040/IJPSR.0975-8232.13\(1\).61-69](http://dx.doi.org/10.13040/IJPSR.0975-8232.13(1).61-69)
- (5) Ahmed, S.; Islam, M. S.; Ullah, B. A review article on pharmaceutical analysis of pharmaceutical industry according to pharmacopoeias. *Orient. J. Chem.* **2020**, *36*, 1-10. <http://dx.doi.org/10.13005/ojc/360101>
- (6) Majidian, M.; Ozcelikay, G.; Cetinkaya, A. Nanomaterial-based electrochemical sensing platform for the determination of Olaparib. *Electrochim. Acta* **2023**, *449*, 142198. <https://doi.org/10.1016/j.electacta.2023.142198>

- (7) Davani, B. Common methods in pharmaceutical analysis. In: Davani, B. (Ed.), *Pharmaceutical Analysis for Small Molecules*, 1st edition. John Wiley & Sons, Inc. 2017. Chapter 3, p 37.
- (8) Michalkiewicz, S.; Skorupa, A.; Jakubczyk, M. Carbon materials in electroanalysis of preservatives: A Review. *Materials* **2021**, *14*, 7630. <https://doi.org/10.3390/ma14247630>
- (9) Wang, J. *Analytical Electrochemistry*, 2nd edition. Wiley-VCH, New York, USA. 2000.
- (10) Hegde, R. N.; Vishwanatha, P.; Nandibewoor, S. T. Voltammetric assessment of 8-Oxoguanine at a nano-structured carbon materials based modified glassy carbon electrode. *Braz. J. Anal. Chem.* **2022**, *9*, 84-93. <http://dx.doi.org/10.30744/brjac.2179-3425.AR-20-2022>
- (11) Qian, L.; Durairaj, S.; Prins, S. Nanomaterial-based electrochemical sensors and biosensors for the detection of pharmaceutical compounds. *Biosens. Bioelectron.* **2021**, *175*, 112836. <https://doi.org/10.1016/j.bios.2020.112836>
- (12) Pushpanjali, P. A.; Manjunatha, J. G.; Hareesha, N. An overview of recent developments of carbon-based sensors for the analysis of drug molecules. *J. Electrochem. Sci. Eng.* **2021**, *11*, 161-177. <https://doi.org/10.5599/jese.999>
- (13) Zhang, M.; Ma, M.; Miao, Z. Coal-based activated carbon functionalized with anionic and cationic surfactants for asymmetric capacitive deionization of nitrate. *Colloids Surf., A* **2023**, *663*, 131054. <https://doi.org/10.1016/j.colsurfa.2023.131054>
- (14) Önal, G. Investigation of the electrochemical properties of vinblastine on boron-doped diamond electrode treated with anodic pre-treatment in anionic surfactant medium. *Diam. Relat. Mater.* **2023**, *133*, 109699. <https://doi.org/10.1016/j.diamond.2023.109699>
- (15) Nabil, A.; Hendawy, H. A. M.; Abdel-Salam, R. A green voltammetric determination of molnupiravir using a disposable screen-printed reduced graphene oxide electrode: application for pharmaceutical dosage and biological fluid forms. *Chemosensors* **2023**, *11*, 471. <https://doi.org/10.3390/chemosensors11090471>
- (16) Sawkar, R. R.; Patil, V. B.; Tuwar, S. M. Electrochemical oxidation of Atorvastatin using graphene oxide and surfactant-based sensor. *Mater. Today. Proc.* **2023**, *74*, 267-273. <https://doi.org/10.1016/j.matpr.2022.08.192>
- (17) Oliveira, L. C.; Rocha, D. S.; Silva-Neto, H. A. Polyester resin and graphite flakes: turning conductive ink to a voltammetric sensor for paracetamol sensing. *Microchim. Acta* **2023**, *190*, 324. <https://doi.org/10.1007/s00604-023-05914-9>
- (18) Weheabby, S.; Wu, Z.; Al-Hamry, A. Paracetamol detection in environmental and pharmaceutical samples using multi-walled carbon nanotubes decorated with silver nanoparticles. *Microchem. J.* **2023**, *193*, 109192. <https://doi.org/10.1016/j.microc.2023.109192>
- (19) Gharous, M.; Bounab, L.; Pereira, F. J. Electrochemical kinetics and detection of paracetamol by stevensite-modified carbon paste electrode in biological fluids and pharmaceutical formulations. *Int. J. Mol. Sci.* **2023**, *24*, 11269. <https://doi.org/10.3390/ijms241411269>
- (20) Stoytcheva, M.; Zlatev, R.; Velkova, Z. The validity of using bare graphite electrode for the voltammetric determination of paracetamol and caffeine. *Int. J. Electrochem. Sci.* **2023**, *18*, 100120. <https://doi.org/10.1016/j.ijoes.2023.100120>
- (21) İslamoğlu, N.; Mülazımoğlu, I. E.; Mülazımoğlu, A. D. Sensitive and selective determination of paracetamol in antipyretic children's syrup with a polyglycine modified glassy carbon electrode. *Anal. Methods* **2023**, *15*, 4149-4158. <https://doi.org/10.1039/D3AY00789H>
- (22) Cortés, K.; Triviño, J. J.; Arancibia, V. Simultaneous voltammetric determination of acetylsalicylic acid, caffeine and paracetamol in pharmaceutical formulations using screen-printed carbon electrode. *Electroanalysis* **2023**, *35*, e202200484. <https://doi.org/10.1002/elan.202200484>
- (23) Islamoglu, N.; Mulazimoglu, A. D. Use of guanine-modified glassy carbon electrode as an electrochemical sensor for the determination of paracetamol. *Bangladesh J. Pharmacol.* **2023**, *18*, 97-104. <https://doi.org/10.3329/bjp.v18i3.66459>

- (24) Prasad, G. V.; Vinothkumar, V.; Jang, S. J. Multi-walled carbon nanotube/graphene oxide/poly(threonine) composite electrode for boosting electrochemical detection of paracetamol in biological samples. *Microchem. J.* **2023**, *184*, 108205. <https://doi.org/10.1016/j.microc.2022.108205>
- (25) Silva, R. M.; Sperandio, G. H.; da Silva, A. D. Electrochemically reduced graphene oxide films from Zn-C battery waste for the electrochemical determination of paracetamol and hydroquinone. *Microchim. Acta* **2023**, *190*, 273. <https://doi.org/10.1007/s00604-023-05858-0>
- (26) Anitta, S.; Sekar, C. Voltammetric determination of paracetamol and ciprofloxacin in the presence of vitamin C using cuttlefish bone-derived hydroxyapatite sub-microparticles as electrode material. *Results Chem.* **2023**, *5*, 100816. <https://doi.org/10.1016/j.rechem.2023.100816>
- (27) Masihpour, N.; Hassaninejad-Darzi, S. K.; Sarvary, A. Nickel-Cobalt Salen organometallic complexes encapsulated in mesoporous NaA nanozeolite for electrocatalytic quantification of ascorbic acid and paracetamol. *J. Inorg. Organomet. Polym.* **2023**, *33*, 2661-2680. <https://doi.org/10.1007/s10904-023-02708-7>
- (28) Urçuk, A.; Yıldız, C.; Bayraktepe, D. E. Electrochemical sensor for simultaneous determination of paracetamol, propyphenazone, and caffeine – Electrodes based on poly(L-cystine)/gold nanoparticles plating on pencil graphite. *Microchem. J.* **2023**, *193*, 109079. <https://doi.org/10.1016/j.microc.2023.109079>
- (29) Porada, R.; Wenninger, N.; Bernhart, C. Targeted modification of the carbon paste electrode by natural zeolite and graphene oxide for the enhanced analysis of paracetamol. *Microchem. J.* **2023**, *187*, 108455. <https://doi.org/10.1016/j.microc.2023.108455>
- (30) Berni, A.; Lahcen, A. A.; Amine, A. Electrochemical sensing of paracetamol using 3D porous laser scribed graphene platform. *Electroanalysis* **2023**, *35*, e202200137. <https://doi.org/10.1002/elan.202200137>
- (31) Liu, X. L.; Guo, J. W.; Wang, Y. W. A flexible electrochemical sensor for paracetamol based on porous honeycomb-like NiCo-MOF nanosheets. *Rare. Met.* **2023**, *42*, 3311-3317. <https://doi.org/10.1007/s12598-023-02349-2>
- (32) Darezereshki, E.; Bakhtiari, F. A novel technique to synthesis of tenorite (CuO) nanoparticles from low concentration CuSO₄ solution. *J. Metall. Sect. B Metall.* **2011**, *47*, 73-78. <http://dx.doi.org/10.2298/JMMB1101073D>
- (33) Fekry, A. M.; Shehata, M.; Azab, S. M. Voltammetric detection of caffeine in pharmacological and beverages samples based on simple nano- Co (II, III) oxide modified carbon paste electrode in aqueous and micellar media. *Sens. Actuators B Chem.* **2023**, *302*, 127172. <https://doi.org/10.1016/j.snb.2019.127172>
- (34) Boltia, S. A.; Kandeel, N. H.; Hegazy, M. A. Analytical eco-scale determination of vortioxetine using advanced electrochemical platform for screen-printed disposable multiwalled carbon nanotube electrode in the presence of an anionic surfactant. *New J. Chem.* **2023**, *47*, 11015-11029. <https://doi.org/10.1039/D3NJ00993A>
- (35) Food and Drug Administration (FDA) *Bioanalytical method validation: guidance for industry*, 2018. <https://www.fda.gov/files/drugs/published/Bioanalytical-Method-Validation-Guidance-for-Industry.pdf> (accessed Jan. 2024).