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The efficacy of the ZnO:α-Fe_2O_3 composites modified carbon paste electrode for the sensitive electrochemical detection of loperamide: A detailed investigation

Noha Al-Qasmi [a,b,1], M. Tahir Soomro [a,1], M. Aslam [a], Ateeq Ur Rehman [c], Shahid Ali [d], Ekram Y. Danish [e], Iqbal M.I. Ismail [a,e], A. Hameed [a,f,*]

[a] *Center of Excellence in Environmental Studies, King Abdulaziz University, Jeddah 21589, Saudi Arabia*
[b] *Department of Chemistry, Faculty of Science, Taif University, Taif, Saudi Arabia.*
[c] *Center for Engineering Research, King Fahd University of Petroleum & Minerals, Dhahran 31261, Saudi Arabia*
[d] *Center of Excellence in Nanotechnology, King Fahd University of Petroleum and Minerals, Dhahran 31261, Saudi Arabia*
[e] *Chemistry Department, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia*
[f] *National Center of Physics, Quaid-e-Azam University, Islamabad 44000, Pakistan*

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ABSTRACT

The efficacy of the ZnO-α-Fe_2O_3 composites as carbon paste electrode (CPE) modifier for sensitive electrochemical detection of loperamide was explored. The composites were synthesized in 1:1, 2:1, and 3:1 (ZnO:α-Fe_2O_3) ratios by the gradual amalgamation of pre-synthesized α-Fe_2O_3 and hydrated gel of Zn^{2+} that later transformed to the ZnO by thermal treatment. The lattice parameters of the composite ZnO and the probable variations in the oxidation states of the components during the adopted coating procedure were assessed by X-ray diffraction (XRD) and X-ray photoelectron spectroscopy (XPS), respectively. The field-emission scanning electron microscopy (FESEM) imaging of the as-synthesized and carbon paste (CP) dispersed composite powders at various resolutions exposed the increased surface coverage of the α-Fe_2O_3 by the ZnO particles with the increasing loading and the uniform distribution of the composite materials in the matrix of carbon paste. Compared to bare CPE, the composites modified CPEs exhibited significantly decreased charge transfer impedance at the electrode/electrolyte interface evaluated by electrochemical impedance spectroscopy (EIS). The sensing ability of the composites modified electrodes for the detection of loperamide in the aqueous medium was investigated. A higher and affectedly improved cyclic voltammetric (CV) oxidation signal of loperamide was noticed at the prepared ZnO:α-Fe_2O_3/CPEs compared to pure components modified CPEs i.e. ZnO/CPE and α-Fe_2O_3/CPE. Based on the EIS and CV investigations, a superior electrochemical performance of (2:1) ZnO:α-Fe_2O_3/CPE was established. Additionally, under optimized experimental conditions of pH, deposition potential, and accumulation time, loperamide was quantified by square wave stripping voltammetry (SWSV) that resulted in the linear calibration ranges from 0.08–1 and 2–10 μmol L^{-1} with detection limits (S/N = 3) of 7.9 and 3.6 nmol L^{-1}. The findings of various electrochemical investigations were correlated to establish the mechanism of charge transport and oxidation of loperamide.

1. Introduction

The development of electrochemical sensors, for the rapid detection of a wide variety of chemical water contaminants, is a well-established area of research with the enormous literature [1–2]. Recently, the metal oxide semiconductors and their composites, owing to high surface to volume ratio, high rate conductivity, adsorption ability, and excellent electrocatalytic capability have attracted pronounced attention for application in electrochemical sensing technology [3–10]. Although, the composites of mixed metal oxide semiconductors also showed better electron transfer kinetics and significantly improved electrocatalytic performances in the electrochemical analysis, however, in comparison to the pure metal oxide semiconductors very few studies are reported in the literature [11–16].

The modified carbon paste electrodes (CPEs), composed of chemical modifiers, graphite powder, and an organic binder, have been widely studied as electrochemical sensors with excellent electrochemical performance owing to their high selectivity, better sensitivity, ease of preparation, reproducibility, and stability [17–23]. Moreover, good detection limits and inherent portability has made the lost-cost chemically

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* Corresponding author at: Center of Excellence in Environmental Studies, King Abdulaziz University, Jeddah 21589, Saudi Arabia.

E-mail addresses: ahfmuhammad@gmail.com, afmuhammad@kau.edu.sa, hameedch@yahoo.com (A. Hameed).

[1] Equal contribution.

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modified carbon paste electrodes as a suitable choice to vast analyte spectrum [24–27]. More recently, application of various semiconductor materials such as titanium oxide (TiO_2), zinc oxide (ZnO), cerium oxide (CeO_2), magnesium oxide (MgO), and iron oxide (Fe_3O_4) as a chemical modifier for carbon paste electrode has been reported [28–39].

Loperamide, which is commercially available as loperamide hydrochloride (4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]-*N*,*N*-dimethyl-2,2-diphenylbutanamide HCl), is an anti-diarrhea drug for the fast and effective relief of diarrhea associated with inflammatory bowel disease [40–41]. Loperamide is a synthetic compound and being related chemically to opioid drugs like morphine [42] which cause physical dependency and addiction. Furthermore, it does have opiate withdrawal symptoms and physiological implications such as constipation, dehydration, nausea, and other types of gastrointestinal discomforts [43–44]. Conventionally, the loperamide in pharmaceutical preparations is analyzed with typical instrumental methods such as spectrofluorometry [45–47], potentiometry [41], conductometry [48], calorimetry [49], high performance liquid chromatography (HPLC) [50], liquid chromatography-mass spectrometry or tandem mass spectrometry (LCMS or LC-MS-MS [51–52], and gas chromatography–mass spectrometry (GC–MS) [53]. Although, the techniques are effective to some extent, however, the intrinsic disadvantage associated require the development of a simple, low-cost, fast, portable, and sensitive method for the determination of loperamide. Since electrochemical detection is an attractive and straightforward alternative to conventional analytical methods for pharmaceutical analysis, the development of electrochemical sensors for pharmaceutical compounds has become an exciting area of research and received enormous scientific attention worldwide. However, as far as we know, there is only one report on the use of especially attractive electrochemical voltammetric methods for the determination of loperamide until today [41].

In the current research work, we synthesized and characterized the composites of ZnO and α-Fe_2O_3 (1:1, 2:1, 3:1 weight ratios), and fabricated the composites modified carbon paste electrodes (ZnO:α-Fe_2O_3/CPEs) for the sensing of loperamide. The bare and composites modified CPEs were electrochemically characterized for charge transfer and catalytic activity. The experimental conditions including SWSV parameters for sensitive detection of loperamide were optimized. The minimum limit for the detection of loperamide was evaluated and the results were correlated to discuss the mechanism of oxidation based detection process. The selective and highly sensitive (2:1) ZnO:α-Fe_2O_3 composite based CPE was finally used for the detection of loperamide in wastewater samples.

2. Experimental details

The α-Fe_2O_3 was synthesized by hydrolyzing the solution of $Fe(NO_3)_3 \cdot 9H_2O$ (Sigma-Aldrich) using KOH as a hydrolyzing base. In a typical synthesis, the appropriate amount of Fe^{3+} ions was stirred with Triton X-100 (0.5% with respect to the weight of Fe^{3+} ions) for 30 min at 100 °C. The solution was hydrolyzed by the dropwise addition of 0.1 M·KOH solution and the pH was maintained at 9. The suspension containing $Fe(OH)_3$ was aged overnight. The resultant precipitates were filtered and washed with deionized water until the neutralization of the filtrate. The precipitates were finally washed with ethanol to remove surfactant and dried in the vacuum oven at 100 °C overnight. The dried powder after fine grinding was calcined at 450 °C for 4 h in the muffle furnace at the heating and cooling rate of 10 °C/min. The ZnO incorporated α-Fe_2O_3 powder was synthesized by hydrolyzing the solution of Zn^{2+} and Triton X-100 by the dropwise addition of 0.1 M·KOH solution to form $Zn(OH)_2$ gel by adopting the similar experimental conditions for α-Fe_2O_3. The appropriate amount of the pre-synthesized reddish α-Fe_2O_3 was added gradually to the hydrated gel under stirring. The suspension of α-Fe_2O_3 and $Zn(OH)_2$ gel was heated at an elevated temperature of 200 °C till the formation of precipitates. The precipitates were filtered, washed, dried, and calcined by adopting the procedure detailed above. The composites with (1:1), (2:1) and (3:1) ratios of ZnO:α-Fe_2O_3 were synthesized. The XRD patterns of the pure (ZnO and α-Fe_2O_3) and composite powders were acquired by Scintag XDS 2000 diffractometer, equipped with a Cu *Kα* radiation source, in 20° to 90° range whereas the XPS analysis was carried out by X-ray Photoelectron Spectrometer (PHI 5000 VersaProbe II, ULVAC-PHI Inc.) in the binding energy range of 0 eV to 1200 eV. The deconvolution and curve fitting explored the probable oxidation states of each component. Field Emission Scanning Electron Microscope (FEI, Quanta FEG 450, Quorum Q150R ES, Quorum technologies Ltd.) was employed to investigate the morphology of the synthesized powders in the as-synthesized form and dispersed in carbon paste.

The modified CPEs were fabricated by packing the sonicated dispersion of modifying materials and the fine carbon powder in the polyether ether ketone (PEEK) electrode body. The surface of the packed electrode was smoothened on a soft paper until the appearance of the glossy surface. In a typical preparation, the 70:30 (w/w) graphite powder (Fluka, 99.9%) and liquid binder (high purity paraffin oil, CDH) were mixed and homogenized to make carbon paste. Initially, the modified electrodes were fabricated by dispersing the 10% by weight of each modifier powder with respect to the weight of the CP. The homogeneous distribution of the synthesized powders in the CP matrix was ensured by sonicating the diluted slurry, using acetone as a solvent, for 60 min. The solvent was removed by evaporation at 60 °C in hot air oven. The effect of the amount of the modifier was investigated by fabricating the electrodes with varying proportions of CP and the modifiers. The lowest background current response was obtained by using the bare CPE in the potential sweep range of 0.0 V and + 1.1 V.

The loperamide hydrochloride (LOP·HCl) (>99%) was purchased from Sigma-Aldrich and used without further purification for electrochemical measurements. A stock solution (1.95 mmol L^{-1}) of loperamide in ethanol was prepared by dissolving precisely weighed the amount of LOP·HCL. The working solutions of desired concentration were prepared in 0.1 mol L^{-1} Britton-Robinson buffer at pH 7 (supporting electrolyte). The real samples were collected from local wastewater treatment plant (WTP) and from immediate wastewater outside of local hospitals (HW) (Jeddah, Saudi Arabia), and were filtered through a 0.22 μm membrane filter to remove particulates. The pH of the real samples was also adjusted to pH 7 with 0.1 mol L^{-1} Britton-Robinson buffer. All the analysis was carried out at the ambient temperature of 22 °C.

The EIS, CV, and SWSV measurements were performed using a modular potentiostat/galvanostat (VSP multi-channel potentiostat, Bio-logic Science Instrument, France) equipped with EC-Lab software for data acquisition and analysis. A three-electrode configuration consisting of CPE or (2:1) ZnO:α-Fe_2O_3/CPE as the working electrode, a Pt wire as a counter electrode, and Ag/AgCl/saturated KCl as a reference electrode was employed. For the measurements, the solutions were deoxygenated by purging nitrogen gas (99.99%) for at least 20 min. The EIS spectra in the form of Nyquist plot were recorded at a forward bias of + 0.23 V in 0.1 mol L^{-1}·KCl containing 2 mM $[Fe(CN)_6]^{3-/4-}$, and at open circuit voltage (OCV) in 0.1 mol L^{-1} pH 7 Britton-Robinson buffer containing 10 μmol L^{-1} loperamide over a frequency range of 0.1 Hz to 100 kHz with an AC amplitude of 10 mV. The EIS spectra were fitted to the Randle's equivalent circuit by using Z-fit (EC-Lab software).

3. Results and discussion

3.1. Materials characterization

The XRD patterns of the as-synthesized materials that included ZnO, α-Fe_2O_3, (1:1), (2:1) and (3:1) ZnO:α-Fe_2O_3 composites are presented in Fig. 1. The XRD patterns of the composite materials appeared as the combination of the individual patterns of pure ZnO and α-Fe_2O_3. Although no observable shift in the peak position was noticed, however, with the increasing surface density, an increase in the intensity of the