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NICKEL-ZINC SUPPORTED ON MESOPOROUS SILICA NANOPARTICLES AND ITS POTENTIAL AS A PARACETAMOL SENSOR

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ABSTRACT

This study aims to synthesize a modified mesoporous silica nanoparticle and evaluate its potential as an electrochemical sensor of paracetamol. Nickel-zinc supported on mesoporous nanoparticles (Ni-Zn/MSN) were successfully prepared by in situ electrolysis method. Ni-Zn/MSN was well characterized by Fourier transform infrared spectroscopy (FTIR), x-ray photoelectron spectroscopy (XPS) and transmission electron microscopy (TEM). The potential of Ni-Zn/MSN as an electrochemical sensor of paracetamol was investigated by employing it into carbon nanotubes paste electrodes (Ni-Zn/MSN/CNTs). Ni-Zn/MSN/CNTs exhibit a good peak resolution of cyclic voltammetry and shows redox process of paracetamol is predominantly diffusion-controlled. Under optimal conditions, Ni-Zn/MSN/CNTs showed a linear concentration-response of paracetamol in the range of 4.0 μM to 0.4 mM with a limit of detection of 0.3 μM. Ni-Zn/MSN/CNTs did not interfere by several foreign ions at 10, 50 and 100-folds excess concentration. A good electroanalytical response indicates that the addition of nanoparticles into carbon nanotubes paste electrode has enhanced the sensing platform of the sensor. The results presented herein provide new perspectives of modified mesoporous silica nanoparticles as a potential nanoparticle in the development of paracetamol sensor.

Keywords: Modified mesoporous silica, Nickel-Zinc, Electrochemical sensor, Paracetamol

INTRODUCTION

Paracetamol or N-acetyl-p-aminophenol is among the most used over-the-counter medications globally due to its antipyretic and analgesic activity [1]. It is most indicated for the alleviation of mild and moderate pain, such as musculoskeletal pain, osteoarthritis, and headache [2]. Despite its therapeutic benefits, overdosing or chronic administration of paracetamol may produce serious hepatic and renal toxicity and hence pose a critical public health issue [3]. Thus, the precise and accurate assay of paracetamol content in drug preparations and biological samples is required for quality control and clinical diagnostics.

In Malaysia, the prevalence of counterfeit and substandard medicines remains a significant public health concern. A 2020 cross-sectional survey conducted in Kuala Lumpur reported that although public awareness was moderate, over 50% of respondents admitted to risky behaviors when purchasing such products, indicating ongoing vulnerability to fake or low-quality drugs [4]. Further, a 2021 paper on substandard and falsified medicines outlined that Southeast Asia continues to experience a high burden of these products, with notable caseloads of contaminated and mislabeled pharmaceuticals in Malaysia and its neighboring countries [5]. Analytical findings underscore this trend: during police raids from January to June 2023, Malaysian authorities seized approximately RM 12.7 million worth of counterfeit medications, spanning dozens of illicit labs producing unregistered and potentially dangerous pharmaceuticals [6].

Conventional analytical methods applied in the determination of paracetamol involve the use of ultraviolet-visible (UV-Vis) spectrophotometry [7], high-performance liquid chromatography (HPLC) [8], and chemiluminescence [9]. Although these methods are highly sensitive and selective, they are beset by various disadvantages. These disadvantages are that they need costly and complicated instrumentation, laborious sample preparation, and very skilled operators. Additionally, these methods are usually unsuitable for on-site or real-time analysis since they are complicated.

To surmount such drawbacks, electrochemical sensors have been presented as promising alternatives for the determination of pharmaceuticals. The sensors provide numerous benefits, such as their low cost, portability, fast response, minimal sample preparation requirement, and the potential for real-time monitoring [10–13]. The utility of nanostructured materials, and more specifically mesoporous silica nanoparticles (MSN), has been highlighted in the improvement of sensor performance with their extremely large surface area, high porosity, and improved physicochemical stability [14]. Also, previous study shows that the introduction of transition metals in mesoporous supports has exerted synergistic effects in enhancing electrocatalytic activity, selectivity, and sensitivity for a range of analytes [15].

However, there is still no report on the study of electrochemical activity of MSN modified with bimetallic for the detection of paracetamol. Hence, the objective of the present study is to synthesize and characterize a zinc-nickel modified mesoporous silica nanoparticle Zn-Ni/MSN)-based electrochemical sensor. The sensor will be assessed on the basis of its electroanalytical activity towards paracetamol determination in relation to sensitivity, selectivity, and stability, with the aim of providing an efficient and useful alternative to conventional analysis methods.

MATERIALS AND METHODS

Materials and Reagents

All reagents employed in the synthesis of Ni-Zn/MSN and subsequent electrochemical experiments were of analytical grade and used as received, without further purification. Ethanol, methanol, *N,N*-dimethylformamide, cetyltrimethylammonium bromide, ethylene glycol, ammonium hydroxide, tetraethyl orthosilicate (TEOS), 3-aminopropyltriethoxysilane (APTES), and disodium phosphate (Na_2HPO_4) were procured from Merck. Monosodium phosphate (NaH_2PO_4), catechol, glycine, uric acid, lactose, sucrose, iron(II) sulfate ($FeSO_4$), sodium chloride (NaCl), and paracetamol were obtained from Sigma-Aldrich. All solutions were prepared using distilled deionized water produced by an EASYpure LF system (Barnstead), which was also used for rinsing the synthesized Ni-Zn/MSN materials. The supporting electrolyte

(0.1 M) phosphate buffer solution (PBS) was prepared by mixing appropriate volumes of Na_2HPO_4 and NaH_2PO_4 stock solutions to the desired pH.

Instrumentations

Electrochemical analyses, including cyclic voltammetry (CV) and Square wave voltammetry (SWV), were carried out using a Gamry Interface 1010B potentiostat (Gamry Instruments, USA). A conventional three-electrode setup was employed, comprising an Ag/AgCl reference electrode (Model MF-2052, Bioanalytical Systems, USA), a platinum wire counter electrode, and a Ni-Zn/MSN/CNTs-modified working electrode. The pH of the solutions was measured using an Orion 720A glass pH electrode (Thermo Scientific, USA). Structural and chemical characterization of the Ni-Zn/MSN material was conducted using a Fourier transform infrared (FTIR) spectrophotometer (Cary 630, Agilent Technologies, USA) and X-ray photoelectron spectroscopy (XPS) system (PHI Quantera II, ULVAC-PHI, Japan). The morphological features of the synthesized material were examined with a transmission electron microscope (TEM) (Model JEM 2100F, JEOL Ltd., Japan).

Analytical Procedure

The experimental workflow for the development of the paracetamol electrochemical sensor begins with the synthesis of mesoporous silica nanoparticles (MSN) via a co-condensation and sol-gel method. The resulting MSN is then subjected to in situ electrochemical modification using nickel (Ni) and zinc (Zn) plates, producing the Ni-Zn/MSN. Ni-Zn/MSN was characterized using FTIR, XPS, and TEM techniques to confirm its structural, compositional, and morphological properties. The Ni-Zn/MSN then combined with carbon nanotubes (CNTs) to fabricate the Ni–Zn/MSN/CNTs paste electrode. This fabricated sensor undergoes electrochemical evaluation using voltammetric methods, which includes cyclic voltammetry and square wave voltammetry, to assess its sensitivity, selectivity, and kinetic behavior. Finally, the sensor's performance was evaluated through detecting paracetamol for its potential application in pharmaceutical and environmental settings. The overall workflow was illustrated in Figure 1.

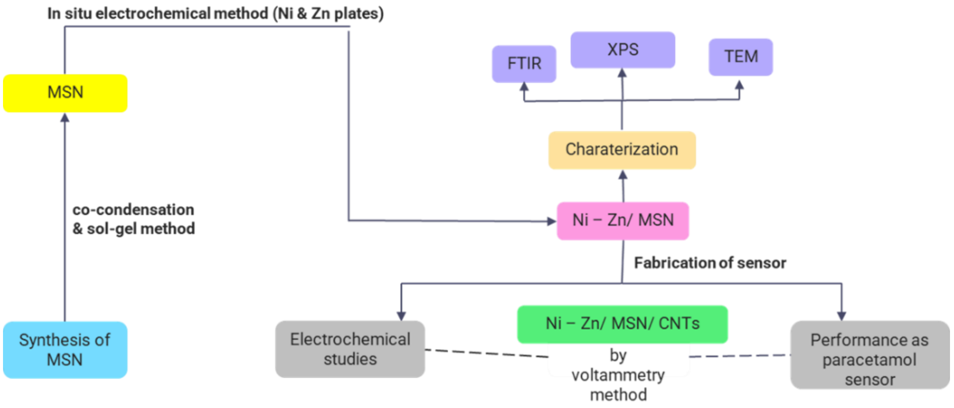


Figure 1. The workflow of this study

Synthesis of Ni-Zn/MSN

Mesoporous silica nanoparticles (MSN) were synthesized via a co-condensation and sol-gel approach. Initially, a solution containing cetyltrimethylammonium bromide, ethylene glycol, and ammonium hydroxide was stirred vigorously at 50 °C for 30 minutes. Subsequently, 1.2 mmol of tetraethyl orthosilicate and 1 mmol of 3-aminopropyltriethoxysilane were introduced into the homogeneous mixture. The reaction mixture was further stirred at 80 °C for 2 hours, then dried overnight at 110 °C. The resulting white MSN powder was calcined at 550 °C for 3 hours to eliminate residual organics and surfactants.

The Ni-Zn/MSN composite was prepared using an in-situ electrolysis method. Platinum (Pt, Nilaco) served as the anode, while zinc and nickel metal plates functioned as the cathode. A total of 30 mL of *N,N*-dimethylformamide (DMF) was used to dissolve tetraethylammonium perchlorate (TEAP), naphthalene, and the synthesized MSN. Electrolysis was carried out at 0 °C under a nitrogen atmosphere, using a constant current density of 480 mA cm^{-2} with continuous stirring. After the reaction, the Ni-Zn/MSN product was collected, heated to 85 °C, and subsequently dried at 110 °C overnight. Final calcination was performed at 550 °C for 3 hours to ensure structural stability and purity.

Preparation of Ni-Zn/MSN/CNTs

To fabricate the Ni-Zn/MSN/CNTs electrode, 100 mg of multi-walled carbon nanotubes (MWCNTs) were mixed with varying amounts (0%, 5%, 7%, and 10% by weight) of Ni-Zn/MSN, followed by the addition of four drops of paraffin oil serving as a binder. The resulting mixture was thoroughly homogenized and tightly packed into Teflon tubes with an inner diameter of 2.0 mm. One end of the tube was polished using soft paper to form a smooth disc-like working electrode surface, while a copper wire was inserted at the opposite end to ensure electrical connectivity. A control electrode was also prepared using the same procedure but without incorporating Ni-Zn/MSN into the MWCNTs paste.

Electrochemical measurements

The electrochemical characterization of Ni-Zn/MSN/CNTs was conducted using the CV technique. The analytical performance of the sensor for paracetamol detection was assessed using SWV technique. All measurements were carried out using a three-electrode system, comprising an Ag/AgCl reference electrode (Model MF-2052) with a fiber junction, a platinum wire as the counter electrode, and either a modified or unmodified multi-walled carbon nanotube (MWCNT) paste electrode as the working electrode. The experimental setup for CV and SWV measurements is illustrated in Figure 2.

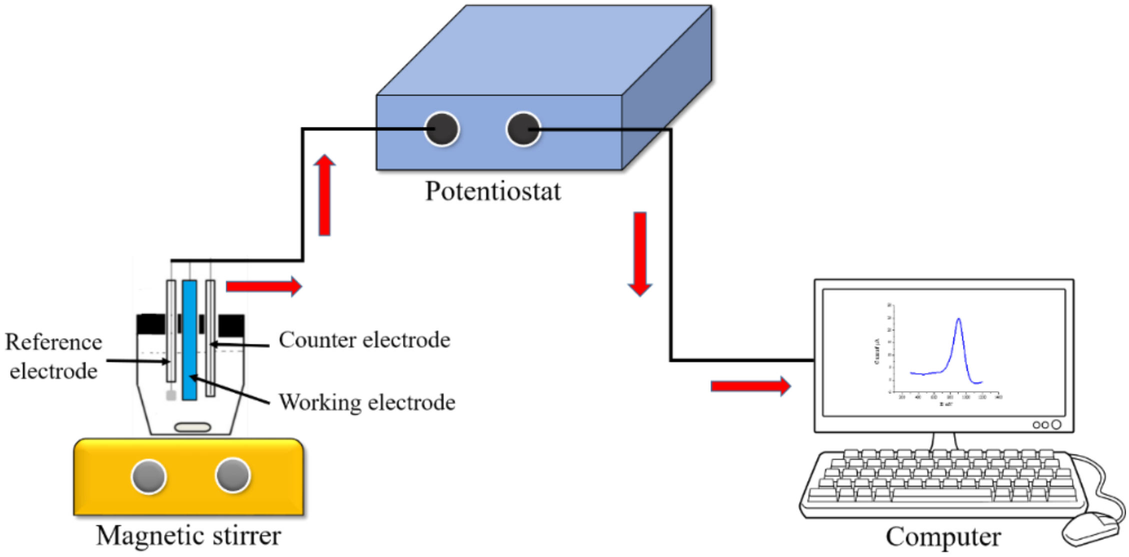


Figure 2. The diagram of a cell for electrochemical measurements

RESULTS AND DISCUSSION

Characterization of Ni-Zn/MSN

Figure 3a shows the FTIR spectra of Ni-Zn/MSN recorded in the range of 4000–400 cm^{-1}. From the FTIR spectra, the absorption band at ~1056 cm^{-1} was assigned to the asymmetric and symmetric stretching vibrations of Si-O-Si. The addition of bimetallic elements (Ni and Zr) has possibly form interaction with Si-O-Si group due to desilication.

The XPS wide scan spectrum, as presented in Figure 3b, confirms the presence of key elements on the surface of the Ni–Zn/MSN composite, specifically Si, O, Ni, and Zn, with their respective binding energies observed at approximately 103 eV (Si2p), 154 eV (Si2s), 532 eV (O1s), 854 eV (Ni2$p_3/_2$), and 1046 eV (Zn2$p_3/_2$). The Si2p spectrum revealed a single well-defined peak centered at 103 eV, corresponding to the Si^{4+} oxidation state in SiO_2, indicating that the silica framework remained chemically stable during the modification process. In the Ni2p region, a distinct peak at 854 eV was observed, attributable to Ni^{2+} species, specifically $Ni(OH)_2$, suggesting the presence of nickel in a hydroxide form rather than in its metallic state. Similarly, the Zn2$p_3/_2$ peak located at 1046 eV is characteristic of Zn^{2+}, confirming the oxidation state of zinc, likely as ZnO or $Zn(OH)_2$. The absence of significant peak splitting features in both Ni and Zn spectra suggests that the metals are predominantly present in their oxidized states rather than in metallic or mixed-valence forms. These findings verify the successful incorporation of Ni and Zn species onto the MSN framework, essential for enhancing the electrocatalytic activity of the synthesized material. Thus, the results confirm that Ni and Zn have been successfully incorporated into the MSN.

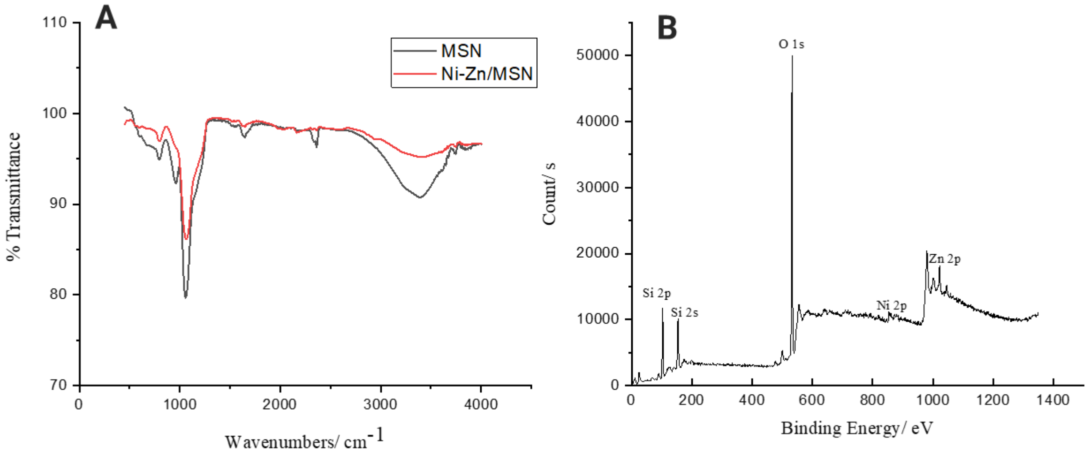


Figure 3. (a) FTIR spectrum of MSN and Ni-Zn/MSN and (b) XPS of Ni-Zn/MSN

Furthermore, Figure 4a shows the TEM image of the synthesized Ni–Zn/MSN, revealing uniformly distributed spherical nanoparticles with a relatively narrow size distribution and an average diameter below 100 nm. The particles exhibit a typical mesoporous structure, characterized by darker contrast regions indicating the presence of internal pores. The inset image in Figure 4a, likely a selected area electron diffraction (SAED) pattern, displays a broad diffraction ring, which suggests the amorphous or semi-crystalline nature of the silica framework [16].

In contrast, Figure **4b** depicts the Ni–Zn/MSN incorporated with multi-walled carbon nanotubes (MWCNTs). The spherical Ni–Zn/MSN particles appear well-attached and interspersed along the fibrous CNT network. This interaction between the nanoparticles and MWCNTs promotes high interfacial contact and uniform dispersion, both of which are crucial for effective electron transport in electrochemical applications.

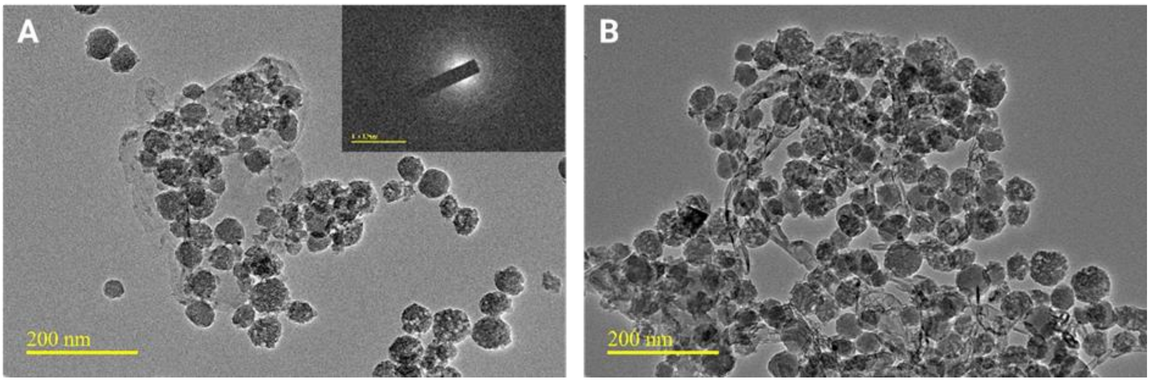


Figure 4. TEM image of (a) Ni-Zn/MSN (inset: SAED pattern) and (b) Ni-Zn/MSN/CNTs

Electrochemical Studies of Ni-Zn/MSN/CNTs

CV results presented in the Figure 5a illustrate the electrochemical response of electrodes fabricated with varying compositions (0%, 5%, 7%, and 10% w/w) of Ni–Zn/MSN incorporated into MWCNTs. Among all tested formulations, the 7% Ni–Zn/MSN composite exhibits the highest anodic peak current at approximately 215 mV, indicating an optimal ratio for enhanced electron transfer and catalytic activity toward paracetamol oxidation. This enhanced response is attributed to the synergistic effect of metal-doped mesoporous silica and the conductive CNT matrix, which together provide increased electroactive surface area, improved porosity, and enhanced redox kinetics. Notably, both lower (0%, 5%) and higher (10%) loading levels resulted in diminished peak currents, likely due to insufficient catalytic sites at low loading and excessive aggregation or reduced conductivity at high loading, which hinders electron transfer [17]. These results confirm that 7% w/w Ni–Zn/MSN offers the best electrochemical performance for paracetamol sensing under the studied conditions.

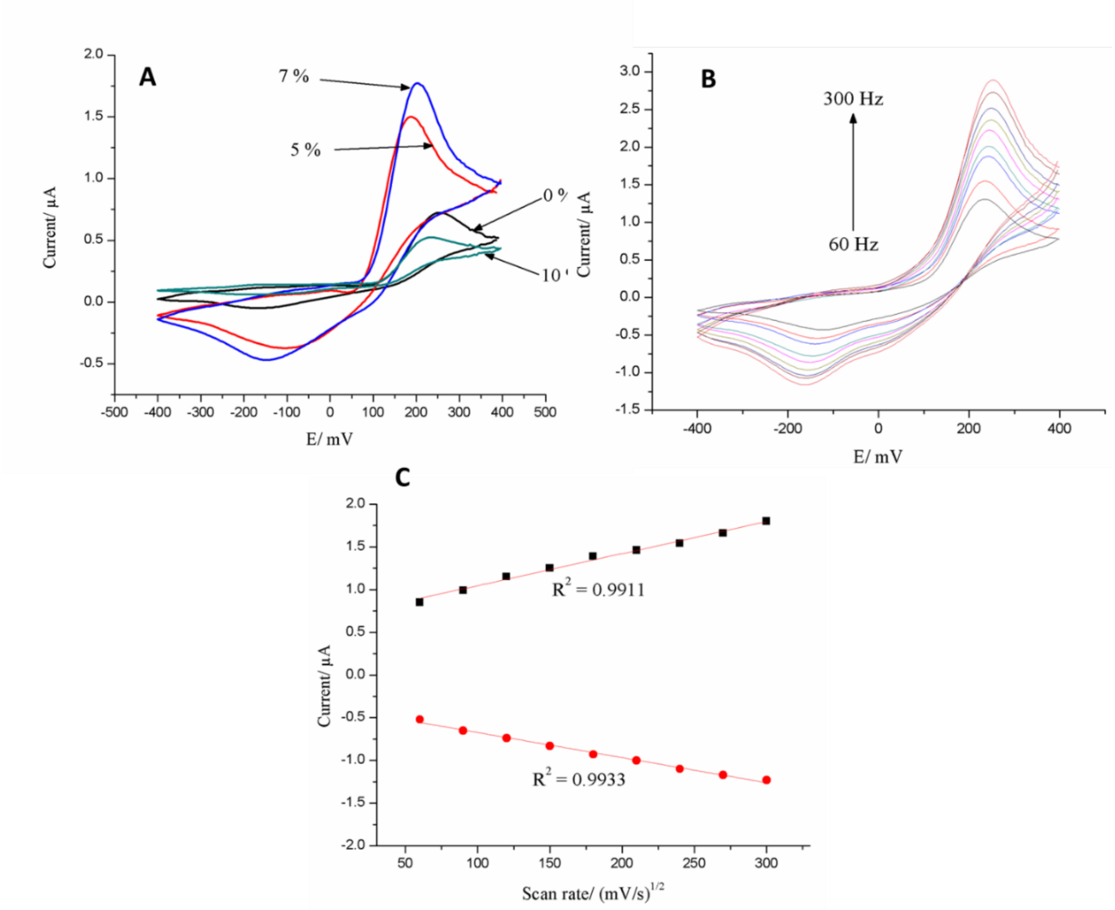


Figure 5. Cyclic voltammogram of Ni-Zn/MSN/CNTs at (a) different composition (b) scan rate. and (c) corresponding plots of peak current versus the square root of the scan rate in the presence of 0.4 mM of paracetamol in 0.1 M PBS (pH7)

CV analysis at varying scan rates (60–300 Hz) for the Ni–Zn/MSN/CNTs electrode demonstrates a progressive increase in both anodic and cathodic peak currents with rising scan rate, as shown in Figure 5b. The corresponding plots of peak current versus the square root of the scan rate (Figure 5c) exhibit excellent linearity ($R^2 = 0.9911$ for anodic and $R^2 = 0.9933$ for cathodic), indicating that the redox process of paracetamol at the modified electrode is predominantly diffusion-controlled. This behavior suggests that the electroactive species are transported to the electrode surface mainly by diffusion, rather than adsorption. The consistent linearity and stability across a wide scan rate range also reflect the robustness of the electrode architecture, where the mesoporous structure of MSN facilitates efficient mass transport, and the incorporation of MWCNTs enhances the electron transfer kinetics [18].

Performance as Paracetamol Sensor

Under optimal condition, the Ni-Zn/MSN/CNTs electrode demonstrated a linear detection range of 4.0 µM to 0.4 mM with a limit of detection (LOD) of 0.3 µM for paracetamol. This linear detection range is useful for the detection of paracetamol in real samples. The enhanced performance can be attributed to the synergistic catalytic effects of Ni and Zn in promoting electron transfer and increasing surface reactivity, as well as the high surface area and conductivity imparted by CNTs [19].

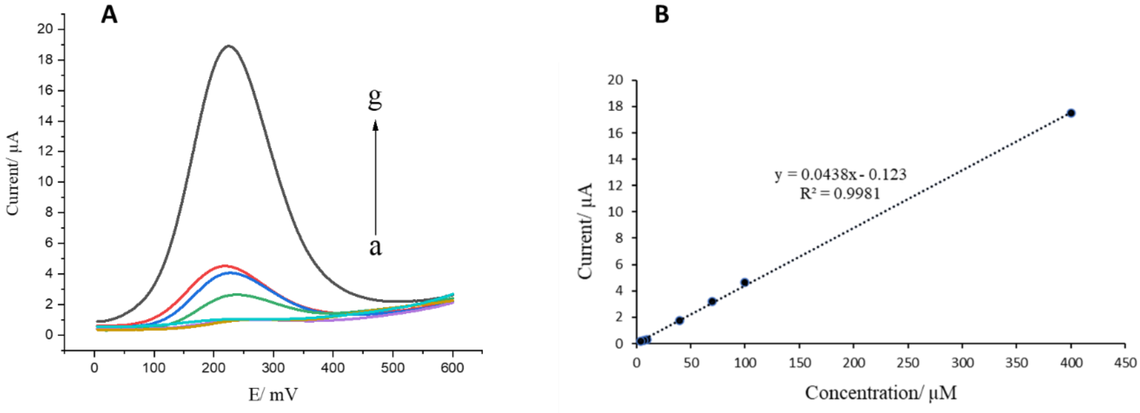
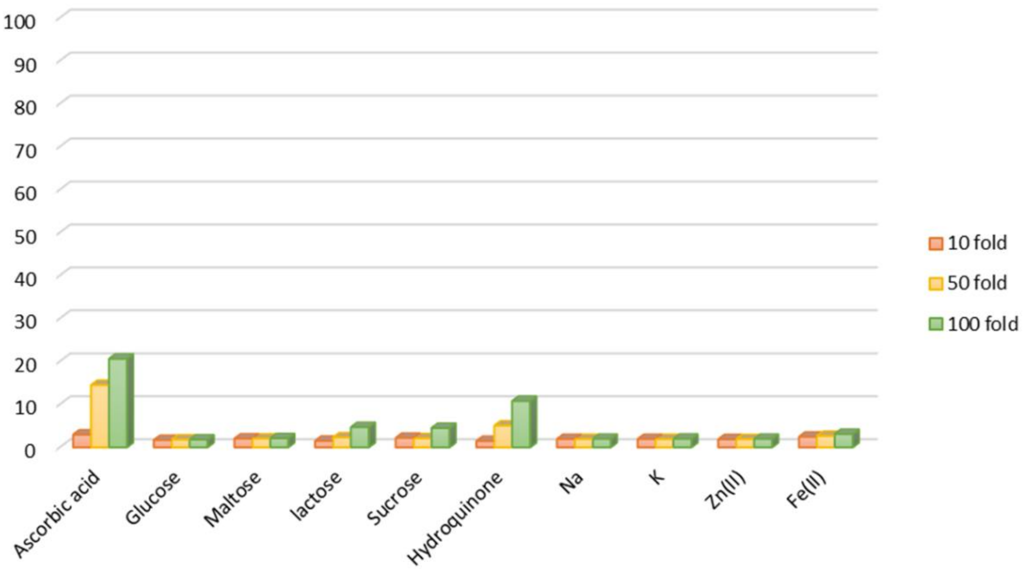


Figure 6. (a) SWV voltammogram of Ni-Zn/MSN/CNTs with additions of paracetamol from 4.0 µM to 0.4 mM and (b) its corresponding calibration plot.

Moreover, the modified sensor showed excellent selectivity toward paracetamol even in the presence of common interfering species, such as ascorbic acid and uric acid, which are often present in biological samples. This high selectivity may result from specific interactions between the analyte and the metal-active sites, as well as the well-defined pore structure of MSN that aids in molecular sieving [20].



CONCLUSION

The Ni–Zn/MSN/CNTs sensor merges the high catalytic activity of Ni-Zn, the structural advantages of mesoporous silica, and the conductivity of CNTs into a platform for paracetamol detection. With a good linear range and detection limit, minimal interference, and ease of fabrication, it addresses both environmental monitoring and public health imperatives. Further analysis may be done through performing analysis of paracetamol in real samples to verify its potential as a practical tool for pharmaceutical quality control and environmental monitoring.

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