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Original Article

Electrochemical Sensing Platform Based on the Modification of Carbon-Ceramic Electrode with Bimetallic Fe/Mn-MOF Applied in the Determination of Nifedipine in Human Serum Samples

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Abstract

Background: Nifedipine, known as a calcium channel blocker, is widely used for the treatment of cardiovascular diseases such as hypertension and angina pectoris. However, its high doses are toxic and may result in a heartbeat, nausea, vomiting, etc.

Methods: In the present research, the bimetallic Fe/Mn-MOF modified carbon-ceramic electrode (CCE) was used for studying the electrochemical behavior and determination of nifedipine. The presence of Fe/Mn-MOF on the surface of the CCE as an efficient modifier caused an increase in the current density of nifedipine oxidation. In this way, optimization of some effective parameters consisting of buffer type, pH, modifier concentration, etc. was successfully performed. Moreover, other analytical parameters including reproducibility, repeatability, stability, and selectivity were investigated.

Results: The relative standard deviation (RSD) of peak current was 3.2 % for 10 μmol.L^{-1} nifedipine. Meantime, the linear range of 1-200 μmol.L^{-1}. Additionally, limit of detection (LOD) and limit of quantification were obtained 0.24 μmol.L^{-1} and 0.82 μmol.L^{-1} respectively. The results showed that the modified electrode has a good electro-oxidation capability for nifedipine. Finally, for investigating the accuracy of the fabricated sensing assay, the determination of nifedipine in drug and human serum samples was performed. The recoveries and the related *RSDs*% were obtained 96.4-102% and 2.2-3.6% respectively.

Conclusion: This modified electrode exhibited appropriate stability, low cost, simple preparation, fast response time, high repeatability, and good sensitivity. The obtained results clearly demonstrate the applicability of the proposed sensing assay in various matrix effects which does not affect the electrochemical response.

Introduction

Due to the increasing obesity rate all over the world where as many as 80% of people do not have enough physical activity, hypertension has become a serious concern for scientists.[1,2] nifedipine (1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-3,5-pyridine dicarboxylic acid dimethyl ester) is one of the most used and prescribed drugs for the management and treatment of hypertension in various medical conditions.[3,4] It is a calcium channel blocker drug that is effectively and widely used for the treatment of cardiovascular diseases such as hypertension and angina.[5] In the human body, nifedipine is mainly converted to the derivative state of nitropyridine, and its normal dosage for treatment is 30 mg.[6] However, nifedipine is poisonous in excess concentration and may have unpleasant moderate to severe consequences. Therefore, it is important to develop efficient methods which can detect nifedipine with high sensitivity, accuracy, and precision.

The methods for the selective detection of nifedipine in the biological fluids are high-performance liquid chromatography (HPLC) coupled with a UV detector,[7] gas chromatography (GC),[8,9] liquid chromatography-mass spectrometry (LC-MS),[9,10] spectrofluorimetry,[11,12] and electrochemical methods.[13,14] However, chromatographic methods have some disadvantages such as the length of time required for sample identification, the high cost, the need for sample pretreatment, the need for trained technicians, and in some cases, the low sensitivity.[15-18] Instead, electrochemical sensors have features such as high selectivity and sensitive, cost-effective, low limit of detection (LOD), wide linear range, appropriate stability, and in-situ analysis.[19-21] These sensors are also used widely

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for the identification and analysis of drug materials.[22-24] Additionally, the presence of the nitrophenyl group in nifedipine, as an electroactive group, led to the development of analytical methods and the identification of nifedipine by electrochemical methods.[25-27]

Modification of the electrode surface is a useful way for highly enhancing the electrochemical signal due to increasing surface area and also electron transfer rate.[28-30] Moreover, by modifying the surface of different electrodes, parameters like selectivity and sensitivity of the target species can be improved.[31] Metal-organic frameworks (MOFs) are formed by the accumulation of ions or metal clusters and organic ligands as metallic ion connectors. MOFs, especially bimetallic MOFs are a class of porous nano-materials that have attracted a great deal of attention in the last years, due to their structure, wide harmonic pore surface area, the large size of their cavities, and adjustable composition.[32-39] Bimetallic MOFs major advantage over monometallic MOFs is the improvement in catalytic properties since bi-metallization improves the original single-metal catalyst's properties and creates a new property.[40] Moreover, bimetallic MOF derivatives have active sites, good conductivity, and high stability.[41]

The purpose of the present research work is to study the electrochemical behavior of nifedipine on the modified carbon-ceramic electrode (CCE) with Fe/Mn-MOF and the determination of nifedipine in human serum samples. Fe/Mn-MOF modifier was synthesized using a direct solvothermal method and the performance of the mentioned bimetallic MOF as a heterogeneous catalyst was evaluated. High sensitivity, simple design, and long-term stability are the prevailing analytical properties of the designed sensor compared with the related studies in this field.

Material and Methods

Reagents and materials

Methyl trimethoxy silane (MTMOS), methanol, ethanol, acetonitrile, hydrochloric acid, and graphite powder were purchased from Merck (Germany) and used without any further purification. nifedipine was purchased from Merck (Germany). The double-distilled water which was used in all solution preparation was purchased from Shahid Ghazi Pharmaceutical Co. All other chemicals were of analytical-grade and were used without further purification.

Instruments and apparatus

The Potentiostate/Galvanostate Autolab PGSTAT 30 (Eco Chemie B.V., The Netherlands) was applied for performing the electrochemical sensing analysis. The electrochemical experiments were performed in a conventional three-electrode cell, at room temperature and the solutions were deoxygenated by nitrogen gas before each approach. The reference electrode was a saturated calomel electrode (SCE) and an auxiliary electrode was a Pt wire. The bare and modified CCE by Fe/Mn-MOF electrodes were utilized as working electrodes in this study. Reference and auxiliary electrodes were purchased from Azar Electrode Co. (Urmia, Iran). Moreover, the composition of bimetallic Fe/Mn-MOF was studied by XRD patterns recorded on an X-ray diffractometer (D500 S) within the range of $2\theta = 2–70°$. For investigating the characterization of the provided Fe/Mn-MOF, Fourier transform infrared (FT-IR) spectra were achieved from Bruker Instruments, Germany, model Aquinox 55. Additionally, for the explanation of the surface morphology, scanning electron microscopy (SEM) and energy dispersive X-ray analysis (EDX) experiments were done on a MIRA3 TESCAN made in the Czech Republic.

Synthesis of bimetallic Fe/Mn-MOF

The related MOF used in this research was synthesized by a solvothermal method like the below: terephthalic acid (4 mmol and 0.67 g), Fe (II) chloride tetrahydrate (4 mmol and 0.80 g), and Mn (II) chloride tetrahydrate (4 mmol and 0.8 g) were respectively dissolved in 20 mL of DMF. In order to obtain a uniform solution, sonication was performed for 30 minutes. Afterward, the hydrofluoric acid (0.8 mL and 5 mL) was added to the solution and the resulting solution was then stirred for 10 minutes. Then, the solution was transferred to a 100-mL autoclave and preserved inside an oven at 150 °C for 3 days. After cooling to room temperature, it was centrifuged (6000 rpm, 10 minutes), and washed with DMF, methanol, and water. After drying and milling the Fe/Mn-MOF composition, it was ready for using.[42]

Preparation of CCE and Fe/Mn-MOF/CCE

In order to prepare CCE with the sol-gel technique, 0.6 mL MTMOS, 0.9 mL methanol, and 0.1 mL hydrochloric acid (0.1 $mol.L^{-1}$) were stirred for 10 minutes to obtain a homogeneous gel solution. In the next step, 300 mg graphite powder was added to the solution and mixed for 5 minutes. Then, the mixture was added into a Teflon tube (with 3 mm I.D. and 3 cm length, and the length of composite in the tube was about 8 mm) and dried for 48 hours at room temperature. The surface of obtained electrode was polished with 800, 2000, 2500, and 3000 grit polishing papers, respectively, and then was rinsed thoroughly with water to yield a shiny surface. In the end, the copper wire was connected to the other end to provide the electrical contact and in this way, the CCE was obtained.

In order to modify the CCE surface with bimetallic Fe/Mn-MOF, 6 mg synthesized Fe/Mn-MOF was added to 1 mL of ethanol. Then it was placed in an ultrasonic bath for half an hour to give a uniform suspension and homogeneity. Subsequently, 10 µL of the fresh prepared solution was dropped on the polished surface of the CCE and allowed to dry at room temperature for 12 hours. Moreover, the fabrication process of the designed sensor has been shown in Scheme 1.

Results and Discussion

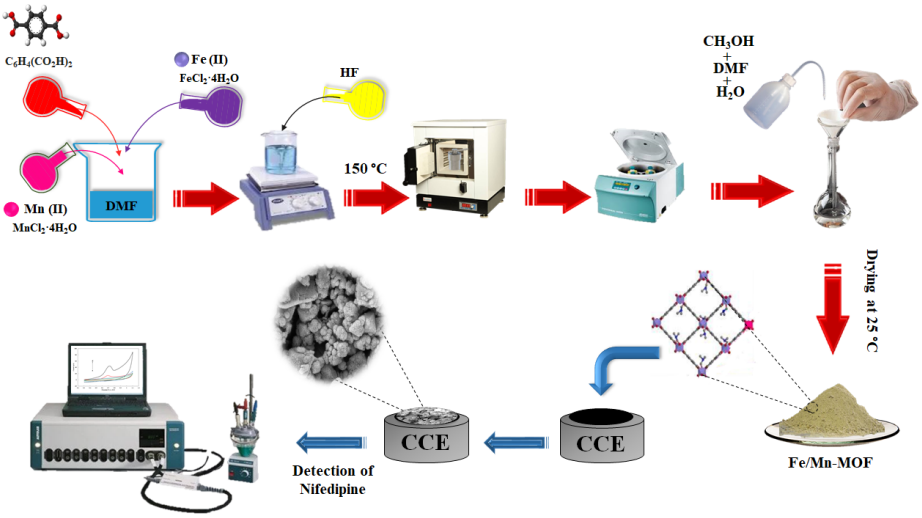
Surface morphology

SEM investigations

SEM is one of the best analytical methods that is used today in many fields. This microscope enables the analysis of chemical, composition, surface, internal microstructures, and biological specimens in micrometer and nanometer dimensions.[43] Figure 1A-D shows SEM images of the surface of bare CCE at a magnification of 5000 times and modified-CCE with a metal-organic framework at magnifications of 10, 50, and 100 times respectively. As shown in Figure 1A, the bare CCE has a nearly flat, scales-like surface with distinct carbon layers due to the reason for the uneven distribution of carbon powder in the silica structure. Moreover, as shown in Figure 1B-D, bimetallic Fe/Mn-MOF owns the diamond-like and octahedron morphology. On the other hand, Fe/Mn-MOF can be used as an effective agent for electrode surface modification due to increasing the surface area of the electrode and porous morphology of the bimetallic. It is seen clearly, a large number of MOFs were successfully deposited on the surface of CCE and uniformly covered the surface of the CCE.

EDX, XRD, and FT-IR analysis

The chemical composition of the Fe/Mn-MOF/CCE electrode was also analyzed by the EDX spectroscopy technique. Figure 1E shows a typical EDX analysis of



Scheme 1. Graphical abstract of the related sensing assay

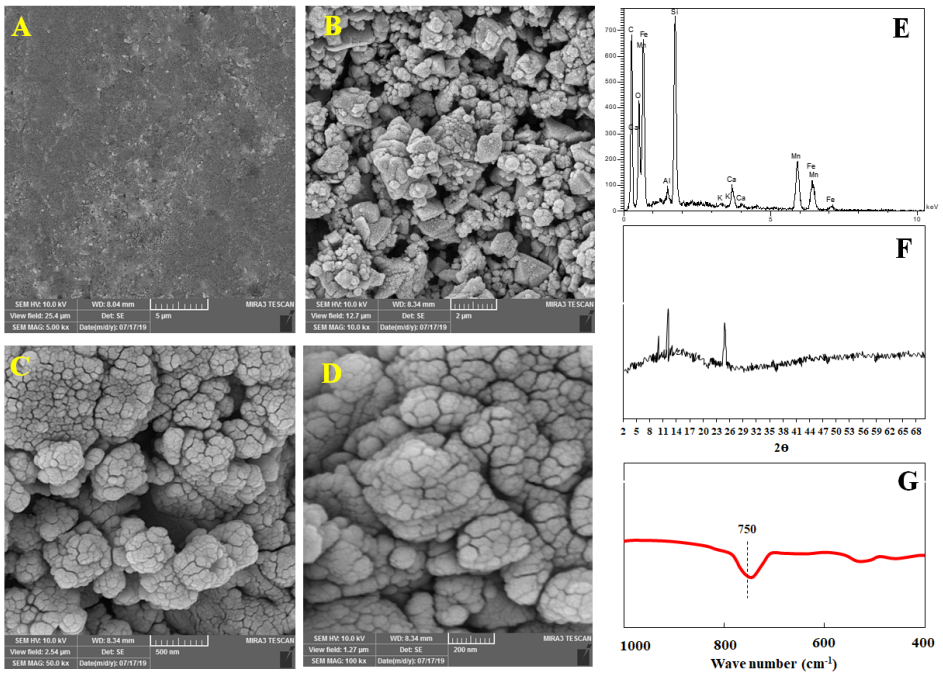


Figure 1. SEM image of (A) bare CCE, and (B, C and D) modified CCE with Fe/Mn-MOF, (E) EDX spectrum of Fe/Mn-MOF/CCE, (F) XRD pattern of the Fe/Mn-MOF, and (G) FT-IR spectrum of the Fe/Mn-MOFs

the modified electrode surface. Fe and Mn peaks could be found in the EDX spectrum which confirms that bimetallic Fe/Mn MOF was successfully deposited on the CCE surface.

The XRD method was used for the analysis of the electrodeposited bimetallic Fe/Mn-MOF on the surface of CCE and the corresponding XRD curve is represented in Figure 1F. The diffraction peaks located at a lower degree demonstrate that the bimetallic MOF has carbonaceous crystal shape. Three diffraction peaks at the values of 23°, 11°, and 8° demonstrate that Fe/Mn has been decorated onto the surface of the electrode in its metallic state. The results confirmed that the obtained XRD pattern is consistent with the sources and the synthesis of the metal-organic Fe/Mn-MOF has been successfully accomplished.

By applying spectroscopy of FT-IR, the synthesized bimetallic Fe/Mn-MOF were studied (Figure 1D). The FT-IR spectrum illustrated that these Fe/Mn-MOF displayed similar peaks in general, as shown in Figure 1G. The typical absorption peaks were observed at 1657, 1560, 1373, 1017, and 750 cm^{-1}, which could be attributed to the vibration of the carboxylate groups.

Electrochemical behavior of nifedipine

To study the electrochemical behavior of nifedipine, the cyclic voltammograms (CVs) of the bare and modified CCE in 10 mL of phosphate-buffered saline (PBS) with pH = 7 was used in the absence and presence of 0.5 $mmol.L^{-1}$ of nifedipine (Figure 2). CVs of the bare CCE in the solution containing nifedipine clearly demonstrated that the presence of a small nose on the voltammograms is related to the electrochemical activity of nifedipine. However, the related peak recorded on the bare electrode was not desirable in terms of peak current intensity, shape, and potential and was unusable for analytical purposes. Consequently, bimetallic Fe/Mn-MOF as an efficient modifier agent was used to increase the peak current and transfer the nifedipine oxide peak potential to more negative values. As illustrated in Figure 2, voltammograms with increased peak current intensity were observed for the nifedipine compared to the bare electrode. These results indicate that the electrode modified with Fe/Mn-MOF shows very good electrocatalytic activity against the nifedipine electro-oxidation and increases the rate of electron transfer between the nifedipine and the surface of the electrode.

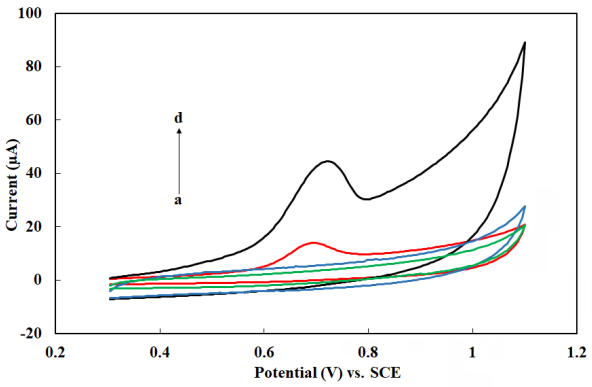


Figure 2. (a) CVs of the bare CCE in PBS, (b) the bare CCE in PBS with 5 $mmol.L^{-1}$ nifedipine, (c) Fe/Mn-MOF/CCE in PBS, and (d) Fe/Mn-MOF/CCE in PBS with 5 $mmol.L^{-1}$ nifedipine at 50 mV s^{-1}

Optimization steps

In the fabrication of the sensor, various parameters affect the electrochemical response of nifedipine, including buffer type**,** modifier (Fe/Mn-MOF) concentration, pH of the solution and scan rate. In order to increase the efficiency and improve the sensitivity of the NIF sensor, the following experimental parameters were optimized.

Selection of buffer type

For this purpose, phosphate and Brighton-Robinson buffers at concentration of 0.1 $mol.L^{-1}$ were used to stabilize the pH at 7. The maximum amount of anodic peak current was obtained for phosphate buffer. Therefore, this buffer was selected as the buffer used to stabilize the pH in the electrochemical study of nifedipine.

Optimization of the Fe/Mn MOF concentration as a modifier agent

To obtain the electrodes with suitable structures, the dependence of the CV response of the electrode modified with bimetallic Fe/Mn-MOF concentration was investigated. For this purpose, suspensions containing 1, 2, 4, 6, 8, 10, 12, and 14 mg Fe/Mn-MOF in 1 mL ethanol were prepared, then 10 µL of obtained suspension was dropped on the surface of the bare CCE. Afterward, each modified CCEs was inserted into an electrochemical cell containing 10 mL of phosphate buffer solution at pH = 7 containing 0.5 $mmol.L^{-1}$ nifedipine, and CVs of each electrode were recorded. As shown in Figure 3A and B, the anodic peak current of the electrode was obtained by applying a modifier with a concentration of 6 mg/mL ethanol has the highest value, after that the current decreased gradually. Accordingly, 6 mg/mL ethanol was used as the optimum Fe/Mn-MOF concentration.

Influence of the pH on electrochemical behavior of nifedipine

The stability of nifedipine and also the peak current intensity and peak potential of the voltammograms are affected by the pH of the solution. For the optimization of the pH, buffer solutions with the pHs of 2-9 were prepared. Since the addition of $H^+$and OH^- to adjust the pH of the buffer solutions at different values causes the ionic strength of the solutions to change, the ionic strength of all solutions was adjusted to a certain value using KCl salt. According to the obtained data, the oxidation peak current reached its highest value at pH = 7 for nifedipine. Therefore, the optimal pH was selected 7 in further investigation.

Calculating Fe/Mn-MOF/CCE surface area

In the case of the modified electrode, an increase in the scan rate results in an increase in the peak current intensity of the CV, which may be proportional to the two factors including υ and $\upsilon^{1/2}$. If the increase in current intensity is proportional to υ, the mass transfer mechanism is based on the adsorption processes, while if the scanning rate is proportional to the $\upsilon^{1/2}$, the mass transfer mechanism is controlled by the diffusion phenomenon.[44] To determine the nature of the anodic current dependent on the oxidation of nifedipine on a CCE with Fe/Mn-MOF, CVs of this electrode in a nifedipine solution at pH = 7 at a concentration of 5 mmol.L^{-1} at the range of 10-600 mV/s was recorded. As it is clear in Figure 4A and B, the changes in the intensity of the current have a linear relationship with the scan rate indicating that the mechanism of mass transfer follows the diffusion process. Moreover, the effective surface area of the electrode was obtained 0.094 cm^2 by the Randles-Sevcik equation (equation 1), which indicates the increased surface area compared to the surface of the CCE (0.071 cm^2).

$$Ip = (2.69 \times 10^5)\, n^{3/2}\, ACD^{1/2}\, \upsilon^{1/2} \qquad \text{Eq. (1)}$$

Estimation of the number of electrons of the nifedipine oxidation reaction

For estimating the number of electrons, the logarithmic dependence of scan rate to potential was investigated. Such a plot for the oxidation of nifedipine at the surface of the CCE modified with bimetallic Fe/Mn-MOF in PBS containing 5 mmol.L^{-1} nifedipine is shown in Figure 4C. Equation (2) describes the logarithm dependence of the scanning rate and the oxidation peak potential:

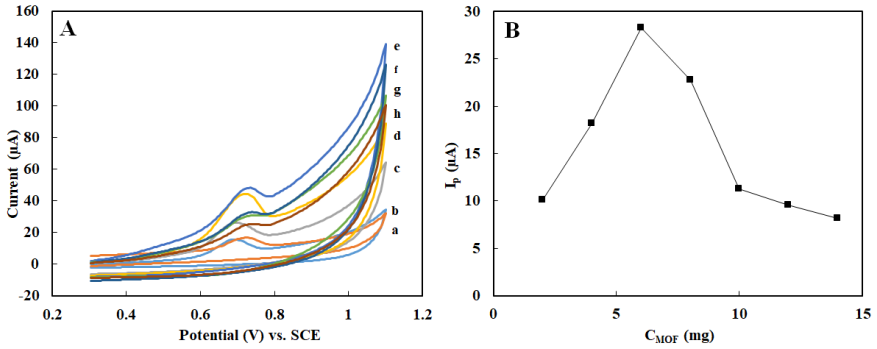


Figure 3. CVs of (A) CCE modified with a) 1, b) 2, c) 4, d) 6, e) 8, f) 10, g) 12, and h) 14 Fe/Mn-MOF dispersed in 1 ml of ethanol in phosphate buffer solution (pH = 7) containing 5 mmol.L^{-1} nifedipine at a scan rate of 50 mV s^{-1}, (B) Plots of anodic peak currents versus the Modifier concentration respectively

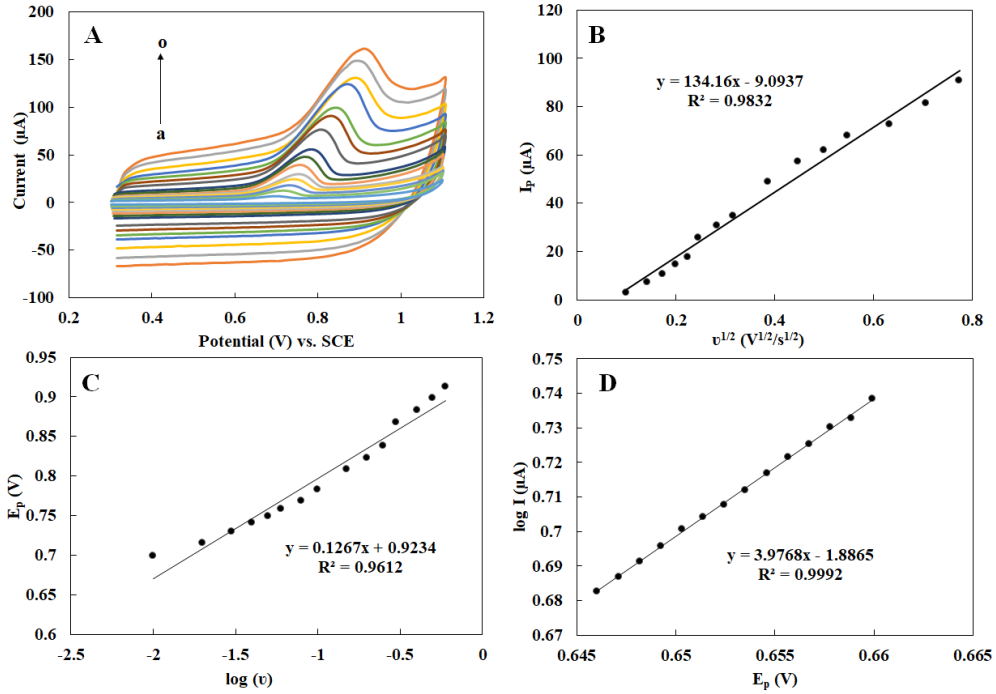


Figure 4. (A) CVs of Fe/Mn-MOF/CCE for 5 mmol.L^{-1} nifedipine in PBS (pH = 7) at different scan rates of 1 to 600 mV.s^{-1}, (B) Dependence of anodic current peak to square of scan rate, (C) Logarithm dependence of nifedipine anodic potential to scan rate on modified electrode in the solution containing 5 mmol.L^{-1} nifedipine in PBS, and (D) A Tafel plot based on a CVs obtained from modified electrode in solution containing 5 mmol.L^{-1} nifedipine at different scan rates in the range of 1 to 600 mV.s^{-1}

$$E_p = \frac{b}{2} \log(\upsilon) + \text{const} \qquad \text{Eq. (2)}$$

In this respect, Ep is the peak potential, b/2 is the slope, $E_p/\log(\upsilon)$ equal to $\frac{2.3RT}{(1-\alpha)n_\alpha F}$ and υ is scan rate. In this research work, α is obtained 0.7672 for nifedipine. A Tafel plot is one of the methods to determine the number of electrons involved in the rate determination step. The Tafel diagram shows the dependence of the current resulting from the electrode processes to applied overpotential on the electrode which is obtained by analyzing the voltammograms drawn at low scan rates. Logarithmic dependence of current potential is known as the Tafel equation (Equation 3).

$$\eta = a - b \log i \quad \text{Eq.} \qquad (3)$$

Where the Tafel slope is equal to. $\frac{2.3RT}{(1-\alpha)n_\alpha F}$

Figure 4D shows the voltammograms of the Fe/Mn-MOF/CCE in PBS (pH = 7) containing 5 mmol.L^{-1} of nifedipine. The Tafel slope for nifedipine is 3.9768 and accordingly n_α was obtained 1 for nifedipine in related electro-oxidation process.

Calculating the diffusion coefficient of nifedipine

Chronoamperometry involves the instantaneous change of the working electrode potential, from the amount in which the oxidation/reduction reaction does not occur, to the potential where the surface concentration of the electroactive species is effectively zero. When the stepped potential is applied to a modified CCE in a carrier electrolyte with a certain concentration of electroactive species, its chronoamperometry response is obtained in the *I-t* curve (Figure 5A), which reduction of current by the time follows by the Catrell equation (Equation 4).[45]

$$I = nFAD^{1/2} C/\pi^{1/2} t^{1/2} \qquad \text{Eq. (4)}$$

n is the number of transferred electrons in the first electrochemical reaction step and C is the concentration of nifedipine (mol/cm^3), D is the diffusion coefficient of electroactive species at fixed temperature (cm/s). The value of 3.248×10^{-6} cm^2/s was obtained as the diffusion coefficient of nifedipine (Figure 5B).

Calibration curve and analytical features of nifedipine

The sensitive differential pulse voltammetry (DPV) technique was used to measure nifedipine at low concentrations. Figure 6A shows the DPVs of the Fe/Mn MOF/CCE for different concentrations of nifedipine. As can be seen, the peak currents of DPV increased linearly (with the linear equation of I = 0.0192C + 0.0984) with increasing of nifedipine concentrations from 0.5 µmol.L^{-1} to 200 µmol.L^{-1}. The LOD for the DPV method was

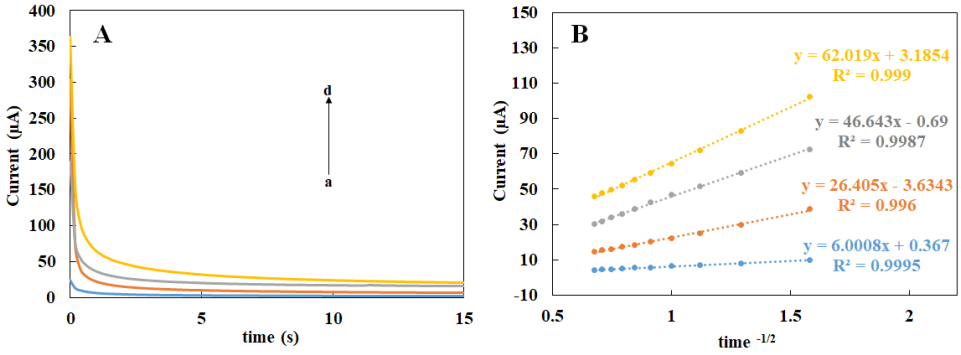


Figure 5. Chronoamperograms obtained on the Fe/Mn-MOF/CCE in 0.1 M PBScontaining 1-4 mM nifedipine, by setting the working electrode potential at 850 mV (A). Plots of I versus $t^{-1/2}$ (B)

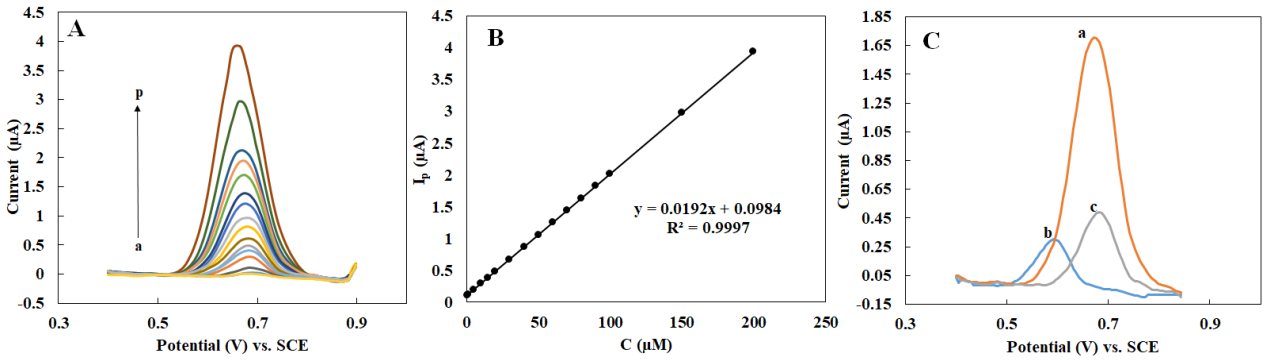


Figure 6. A) DPV voltammograms of the modified electrode in different concentrations of a) 0.5, b) 1, c) 5, d) 10, e) 15, f) 20, g) 30, h) 40, i) 50, j) 60, k) 70, l) 80, m) 90, n) 100, o) 150, p) 200 in 0.1 M of PBS (pH = 7) and scan rate is 10 mV/s. B) Calibration curve. (C) The voltammograms of a) nifedipine, b) Dehydronifedipine (decomposition product), c) the mixture of nifedipine and Dehydronifedipine (concentration of 80 µmol.L^{-1})

calculated to 0.247 μmol.L^{-1} using the calibration curve. The LOD was obtained using equation 5:

$$y_{LOD} = 3S_{y/x} + y_b. \quad \text{Eq. (5)}$$

While y_b is the signal of the blank solution (here intercept of calibration curve), $S_{y/x}$ is the standard deviation of the blank solution (here standard deviation of the calibration curve). Additionally, the limit of quantification (LOQ) was obtained as 0.82 μmol.L^{-1} by equation 6 :

$$y_{LOD} = 10S_{y/x} + y_b \quad \text{Eq. (6)}$$

The obtained results clearly demonstrate that the excellent performance of the bimetallic Fe/Mn-MOF modified CCE toward the reduction of nifedipine makes it a highly suitable sensor for nifedipine determination.

Table 1 summarizes the analytical features of the proposed electrochemical sensor in comparison with other modified electrodes for sensing purposes. As clear, the LOD of our proposed sensor is less than other alike electrodes and also the related linear range is wider than the majority of them. The obtained analytical features show the superiority of the prepared sensor compared to the same ones.

Reproducibility, stability and selectivity

In order to test the reproducibility and stability of the sensor, 5 modified electrodes were prepared independently by the same mentioned way and the investigations were performed. The relative standard deviation (RSD) of peak current was 3.2 % for nifedipine 10 μmol.L^{-1} and also repeatability of the fabricated sensing assay was performed. The repeatability of the fabricated genosensing assay, *RSD%* for five successive measurements of 10 μmol.L^{-1} nifedipine was 2.3%. The *RSDs%* of the obtained electrochemical responses for reproducibility and repeatability steps clearly demonstrate satisfactory values for the novel analytical genosensor. The long-term stability of the sensor was also examined. After storing for three weeks, the peak currents retained 96.3% of its initial value.

Table 1. Comparison of the proposed method with other voltammetric methods for determination of nifedipine

Type of electrode	Technique	Linear range (μmol.L^{-1})	Detection limit (μmol.L^{-1})	Reference
Activated GCE	CV LSV	80-1000	-	[46]
AgNPs/GCE	DPV	0.8-60	0.72	[47]
CuO NPs/CP	DPV	12-96	1.12	[48]
$BiVO_4$–Bi_2O_3/ITO	DPV	50-800	0.459	[49]
BDE	DPV	2-41	0.93	[50]
Fe/Mn-MOF/CCE	DPV	0.5-200	0.246	Present work

LSV, Linear sweep voltammetry; BDE, Boron-doped diamond electrode; CV, cyclic voltammogram; DPV, differential pulse voltammetry; GCE, Glassy carbon electrode.

In addition, the selectivity of this sensor was also investigated. For 10 μmol.L^{-1} nifedipine, 1000-fold Cl^-, NO^{3-}, $Mg^{2+}$and Zn^{2+}, 100–fold glucose, ascorbic acid, citric acid and urea, 70–fold uric acid and dopamine did not show interference. Moreover, selectivity of the proposed sensing assay was proved by comparing the voltammograms of nifedipine and its main metabolite dehydronifedipine. In order to prepare the dehydronifedipine, nifedipine solution was exposed to UV radiation (366 nm) for 14 h. In the voltammogram of this solution, the reduction peak of nitro group shifted to more negative potential comparing with nifedipine (Figure 6C). Addition of dehydronifedipine increased the peak current at potential of 595 mV. Therefore, it has been concluded that nifedipine could be determined in the presence of its metabolite by the proposed method. The obtained results indicate that the sensor possessed desirable reproducibility, stability and selectivity.

Analysis of the spiked samples

To evaluate the applicability of the Fe/Mn-MOF/CCE, the recovery tests of nifedipine were determined in the pharmaceutical and human serum samples by using the standard addition technique. The reduction peak current of nifedipine was measured by DPV. Six parallel experiments are carried out for all measurements. The results obtained from the pharmaceutical and human serum samples are shown in Table 2. The recoveries were ranged between 98.6% and 102.0% for the pharmaceutical samples and 96.4% and 101.4% for the human blood serum samples, indicating that this method can be efficiently used for the determination of nifedipine in real pharmaceutical and serum samples.

Conclusion

Nifedipine is extensively used in the treatment of cardiovascular diseases such as hypertension and angina pectoris. In this research MOFs were used as an efficient modifier for studding of the electrochemical behavior and determination of nifedipine. The linear range of 1-200 μmol.L^{-1} and LOD of 0.24 μmol.L^{-1} was obtained for nifedipine that indicates the capability of modified electrode for determination of nifedipine. Another advantages of the related modified electrode are high reproducibility and repeatability, good sensitivity, and

Table 2. Determination of nifedipine in human serum and pharmaceutical sample

Sample	Added (μmol.L^{-1})	Found (μmol.L^{-1})	Recovery %	RSD %
Pharmaceutical sample	2.5	2.49	99.68	3.4
	5	4.93	98.60	2.2
	10	10.20	102.00	2.7
Human serum	2.5	2.41	96.40	2.4
	5	4.88	97.60	3.1
	10	10.14	101.40	3.6

appropriate stability. Also, the performance of the MOF (Fe/Mn) modified CCE was studied for nifedipine determination in the human serum sample successfully and recoveries showed that the related sensor assay is an appropriate one for determining and measuring the nifedipine in real samples. The obtained results clearly demonstrate that this fabricated sensing assay provides a desirable platform for determination of nifedipine and other significant analytes in real samples and biological medium.

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Data curation: Mir Reza Majidi.
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Investigation: Fatemeh Maleki.
Methodology: Fatemeh Maleki.
Software: Reza Fadakar Baje Baj.
Supervision: Mir Reza Majidi.
Validation: Reza Fadakar Baje Baj.
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The author(s) declare that they have no competing interests.

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All data generated or analyzed during this study are included in this published article.

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