



Competitive adsorption and selective sensing of dopamine over epinephrine and norepinephrine on MOF copper seed composite-based probe

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ABSTRACT

The reticular hydrothermal technique was employed in the fabrication of Zn-based MOFs. The synthesis of MOF-Cu seed has been accomplished from Zn-MOF-CuCl-OLA (oleyl amine) through the solvothermal method. The crystalline defects were diminished by copper seeds, thereby improving the electrochemical selectivity towards dopamine (DA). The MOF-Cu-GCE exhibited more virtuous selectivity for DA over epinephrine (EP), norepinephrine (NE), and other chemical analogs and inorganic salts. This unique selectivity is ascribed to the exterior modification of Cu⁰ to boost the adsorption of DA onto MOF-Cu-GCE through soft-soft interaction and aromatic functionality. Quantitative sensing of dopamine by MOF-Cu-GCE was achieved in the linear range of 50–1100 nM in HSA-PBS with a detection limit of 9.28 nM. Also, the MOF-Cu-GCE demonstrated excellent stability and reproducibility. This research work is a footing for the emergence of a probe for DA based on the hard-soft acid-base principle (HSAB).

1. Introduction

Catecholamine is a neurotransmitter that has a catechol and a primary or secondary amine chain. The catechol ring structure is the backbone of dopamine (DA), epinephrine (EP), and norepinephrine (NE) which are generally present in the mammalian central nervous system (CNS). Among these, DA plays a crucial role in coordination and voluntary activities. Whereas EP and NE have an integral role in the body's fight or flight response. Carlson et al. (1958) reported DA as a neurological messenger generating impulses in between neurons [1,2]. Hence, several neurological disorders can be diagnosed through the determination of DA concentration in the body fluids. Thus, the development of selective, sensitive, and simple methods for the determination of DA is crucial. Recently, various methods have been developed for the selective determination of DA. Liquid chromatography, gas chromatography, micro-dialysis, fluorescence, and electrochemistry are some of them [3–5]. Among them, the electrochemical method of sensing has attracted wide attention due to its high sensitivity, convenience, speed, and reproducibility [6,7]. As well known, DA, EP, and NE consist of a catechol unit that differs structurally only in their amine chain [8]. DA consists of a primary amino ethyl, and the latter contains a beta-hydroxy secondary and primary amine chain. Due to the structural analogy, interference of EP, NE, and DA in body fluids gives a redox peak current

at the glassy carbon electrodes (GCE). So, developing a probe capable of detecting exclusively DA in the presence of EP and NE would represent a paradigm shift in biosensing.

In recent decades, more research has been carried out in the field of metals, crystalline and amorphous carbon materials, and other polymers as electrochemical sensors [9,10]. Among them, metal-organic framework (MOF) and metal nanoparticles are promising porous crystalline polymers having a large surface area, tunable framework, and mechanical strength [10,11]. A highly conjugated, crystalline, and charge-transporting material with minimal defects is necessary for the preparation of a conductive composite [12,13]. The degree of orbital overlap between transporters and carriers within the molecular building blocks influences the phenomenon of charge delocalization. Band-like and hopping are the two main charge transfer mechanisms in solid-state-ordered porous materials (SSOPMs) [12]. In hopping mode, electrons or holes move by bouncing between adjacent, unbounded sites where the charge carriers are localized. Meanwhile, in ballistic transport, continuous energy bands exist between neighboring units, facilitating charge transport. In brief, the orbital overlap between the electron transporters and carriers in the building blocks is essential for charge delocalization [12–14]. Among the pore modifiers, copper (Cu) is often used to enhance electrical conductivity. Moreover, Cu is a better substitute for gold (Au) and platinum (Pt) due to its cost-effective nature

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than any other noble metals [15,16]. Also, Cu has been recently studied as a DA sensor due to its similar physical and chemical properties to Au and Pt. Therefore, our research team is always curious about investigating the synthesis of DA-specific MOF-Cu composites.

In the realm of neurotransmitter detection, conventional methods such as immunoassays and chromatographic separation, along with various detection techniques, have been employed for the selective identification of DA in the presence of NE and EP. Unfortunately, these approaches are often time-consuming, and expensive, and involve the use of toxic reagents, leading to flawed results in experiments. For instance, some methodologies utilize metal ions and leachable toxic organometallic complexes to modulate photoluminescence and redox peaks for DA sensing. In response to these challenges, our research group developed a non-leachable zinc-based MOF. We further enhanced its properties through interior and exterior modification with copper seeds around the MOF. The incorporation of copper onto the rod-shaped MOF imparted a highly conductive nature, and the soft basic characteristics of copper facilitated the adsorption of DA onto the MOF-Cu composite.

The electrochemical reaction process of DA is quasi-reversible, distinguishing it from the irreversible oxidation process of EP. According to the Electron Transfer-Coupled Chemical (ECC) mechanism proposed by Hu et al., pH-dependent electrochemical sensing involves a two-electron oxidation reaction of catecholamines on modified electrodes, leading to the formation of o-quinone (OQ) [8,47]. The OQ then undergoes intramolecular cyclization and internal oxidation-reduction, resulting in leucoaminochrome (LAC). The intramolecular cyclization rates for each catecholamine ($k_{DA} = 0.13 + 0.05 \text{ s}^{-1}$, $k_{NE} = 0.98 + 0.52 \text{ s}^{-1}$, and $k_{EP} = 87 + 10 \text{ s}^{-1}$ at pH = 7.4) differ in phosphate-buffered saline (PBS) [47]. LAC subsequently undergoes a homogenous reaction with another OQ, leading to an additional two-electron oxidation to amino chrome (AC), while the OQ reverts to the catechol form. AC, with an $E_{1/2}$ value of about -0.207 V vs Ag/AgCl (sat KCl) for EP, can also undergo a two-electron reaction. The differences in the rate constants for the intermolecular cyclization reaction, attributed to the presence of methyl and β -hydroxy groups in EP and NE, facilitate the selective sensing of DA. Additionally, the steric hindrance of EP and NE is higher than that of DA, contributing to their reduced adsorption on suitable glassy carbon electrode (GCE) surfaces. Moreover, the weaker Lewis base nature of DA, owing to its primary and secondary amine chains, positively influences its adsorption on the MOF-Cu surface.

Herein, we used zinc (Zn) and aromatic polycarboxylate ligands for the MOF synthesis [17]. Also, a seed-mediated growth approach is adopted for the incorporation of Cu into the MOF pores and surface [16]. Zn and aromatic polycarboxylate ligands are virtuous building blocks for the construction of MOFs. Among them, 1,2,4,5-benzene tetracarboxylic acid (H_4btca) and $Zn(NO_3)_2 \cdot 6H_2O$ -based MOF have strong coordination bridges and have tunable ferro or antiferromagnetic exchange [17]. Moreover, the COO^- and aromatic framework of the H_4btca -based MOF (Zn MOF) form a π - π stacking interaction towards DA [14]. The significance of this study lies in its innovative approach to selectively sensing DA amidst the structural analogs EP and NE. Typically, in DPV analysis, DA, EP, and NE exhibit similar redox characteristics due to their structural similarities. However, our work introduces a MOF-Cu seed-based MOF designed specifically for the selective detection of DA in the presence of EP and NE. The hydrothermal preparation method employed in this research, along with the use of non-toxic copper modification and the non-leachable properties of the MOF, contribute to an environmentally friendly synthesis procedure. This approach not only ensures the selectivity of the sensing mechanism but also aligns with sustainable and eco-friendly principles in material synthesis.

In this work, a seed-mediated growth approach has been developed for the preparation of Cu in the Zn-based MOF. Besides, the soft-soft interaction between nitrogen and Cu^0 selectively adsorbs the primary ethyl part of DA. This scheme provides a new pathway to improve the defects in the crystal phase of MOF using copper seeds and thereby enhance the electrochemical selectivity towards DA. For the physical

and chemical properties, we employed SEM, EDAX, XRD, FTIR, Raman, and XPS characterizations. The electrochemical performance of the several modified GCEs was studied using cyclic voltammetry (CV), differential pulse voltammetry (DPV), and electrochemical impedance spectroscopy (EIS).

2. Experimental section

2.1. Chemicals and reagents

Zinc nitrate hexahydrate [$Zn(NO_3)_2 \cdot 6H_2O$], copper (I) chloride [CuCl], copper (II) sulfate pentahydrate [$CuSO_4 \cdot 5H_2O$], sodium phosphate [Na_3PO_4], sodium nitrate [$NaNO_3$], magnesium nitrate hexahydrate [$Mg(NO_3)_2 \cdot 6H_2O$], sodium sulfate [Na_2SO_4], 1,2,4,5-benzene tetracarboxylic acid (H_4btca) [$C_{10}H_6O_8$], hexaamineruthenium-(III) chloride [$Ru(NH_3)_6Cl_3$] (98%), potassium ferrocyanide [$K_4[Fe(CN)_6]$] (98%), dopamine hydrochloride [$C_8H_{11}NO_2 \cdot HCl$], epinephrine [$C_9H_{13}NO_3$], norepinephrine hydrochloride [$C_8H_{12}ClNO_3$], aspartic acid [$C_4H_7NO_4$], citric acid [$C_6H_8O_7$], cysteine, [$C_3H_7NO_2S$], glucose [$C_6H_{12}O_6$], glutamine [$C_5H_{10}N_2O_3$], histidine [$C_6H_9N_3O_2$], γ -amino butyric acid (GABA) [$C_4H_9NO_2$], ammonium hydroxide [NH_4OH], 5-amino valeric acid [$C_5H_{11}NO_2$], oleyl amine [$C_{18}H_{37}N$] and toluene [C_7H_8] were obtained from Sigma Aldrich. Potassium chloride [KCl] was purchased from Emsure, while hydrochloric acid (HCl) and ethanol were obtained from Duksan, South Korea. Deionized water and phosphate-buffered saline (PBS, 0.01 M, pH 7.4) were used for sensing experiments.

2.2. Electrodes and instruments

All the electrochemical experiments were conducted in a three-electrode system with glassy carbon as the working electrode (WE) (0.07 cm^2). We used coiled Pt wire (ALS Company) as the counter electrode (CE) and saturated Ag/AgCl as the reference electrode (RE). Before each casting, GCE was polished with alumina powder ($0.05 \mu\text{m}$), followed by cleaning with ethanol and distilled water. Electrochemical measurements such as CV, DPV, and EIS were carried out using the WizMac WizEIS-1200 Premium voltammeter at room temperature.

2.3. Electrochemical characterization of various modified GCEs

In the absence of a pathological state, the pH of the human body is around 7.4. Our group investigated the sensing and interference behavior of the DA towards the modified electrode at a pH of 7.4. We characterized the electrochemical behavior of modified GCE in PBS and HSA-PBS at various concentrations of DA. In addition, we performed a comparison experiment using Cu, MOF, and MOF-Cu-modified GCE at a fixed concentration of DA in PBS. Electrochemical characterization measurements of MOF-Cu-GCE were conducted in PBS (1 mM, pH = 7.4). Also, 1 mM $Ru(NH_3)_6Cl_3$ was used as the redox indicator for the scan rate analysis. We used 1 mM PBS (pH = 7.4) to test the MOF-Cu-GCE's impedance response at frequencies from 0.1 Hz to 10^5 Hz with an amplitude of 10 mV. HSA-PBS solution was prepared by adding 10 mg of HSA to 100 mL of PBS (1 mM PBS). Likewise, we electrodeposited copper on the MOF-GCE surface for the preparation of Cu/MOF-GCE. The electrolyte solution was prepared from distilled water containing 1 mM $CuSO_4$, and the redox reaction was carried out from -0.6 to 1 V at a 20-mV scan rate and three cycles.

2.4. MOF, Cu, and MOF-Cu composite preparation

Zn-based MOF has been prepared according to the previous literature through a minor modification [17,14]. $Zn(NO_3)_2 \cdot 6H_2O$ (0.5 mM) and 1, 2,4,5-benzene tetracarboxylic acid (PA) (0.5 mM) were separately dissolved in 5 mL of distilled water, followed by the addition of PA solution to the stirring $Zn(NO_3)_2 \cdot 6H_2O$ solution in a 20 mL Teflon-lined vessel. To the reaction mixture, 0.5 mL of $NH_3 \cdot H_2O$ and distilled water (7.5 mL)

were added. The reaction mixture was subjected to heating in an autoclave at 110 °C for 48 h. The colorless crystal obtained was collected for water wash and centrifugation for 5 min at 5000 rpm.

Copper was prepared from the CuCl-OLA mixture based on the previous reports [15]. The 25 mg of CuCl was dispersed in 5 mL of OLA in a 100-mL glass vial, followed by sonication at room temperature for 10 min. The mixture was then heated to 170 °C for 61 h while stirring. The solution turns a reddish-brown color, indicating the reduction and precipitation of Cu. The temperature of the reaction mixture was decreased to room temperature step by step without stirring. The precipitated Cu was washed three times by adding 30 mL of toluene, followed by sonication for 10 s and centrifugation at 8000 rpm for 5 min. The entire process was repeated four times. The collected sample was vacuum-dried at 60 °C and stored in a vacuum desiccator for further experiments and characterizations.

The MOF-Cu composite was synthesized by blending 25 mg of Cu(I) Cl with 50 mg of previously prepared MOF in 5 mL of OLA in a 100 mL glass vial (as illustrated in Scheme 1 and Fig. S1(a-c)). The entire blend was sonicated for 10 min at room temperature. The mixture was then heated to 170 °C for 61 h while stirring. The solution turns a reddish-brown color, indicating the reduction and precipitation of Cu on the MOF surface. The temperature of the reaction mixture was gradually decreased to room temperature without stirring. The obtained MOF-Cu composite was subjected to three wash cycles by adding 30 mL of toluene, followed by 10 s of sonication and subsequent centrifugation at 8000 rpm for 5 min. This washing process was repeated four times. The composite was vacuum-dried at 60 °C for 24 h and stored in a vacuum desiccator for further experiments and characterizations.

3. Results and discussion

3.1. Morphology and crystallinity of the prepared MOF and MOF-Cu composites

The surface morphology of the MOF and MOF-Cu was investigated using SEM techniques equipped with EDAX. Fig. 1 (a and b) displays the dimension of the zinc MOF nanorod obtained by heating the reaction mixture at 110 °C for 48 h. The prepared nanorod has a straight, four-twinned structure and a tetragonal cross-section with a mean width and height of 1.4 and 1.45 μm , respectively. TEM analysis on the Zn-MOF revealed a morphology analogous to that observed in SEM analysis (Fig. S1 d & e). The synthesized MOF exhibits a nanorod structure

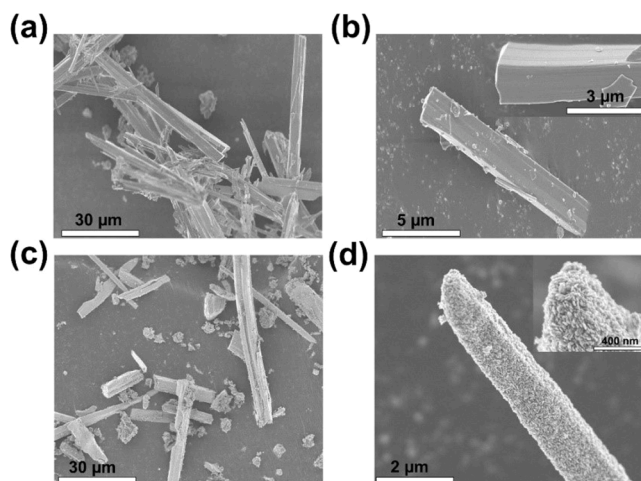


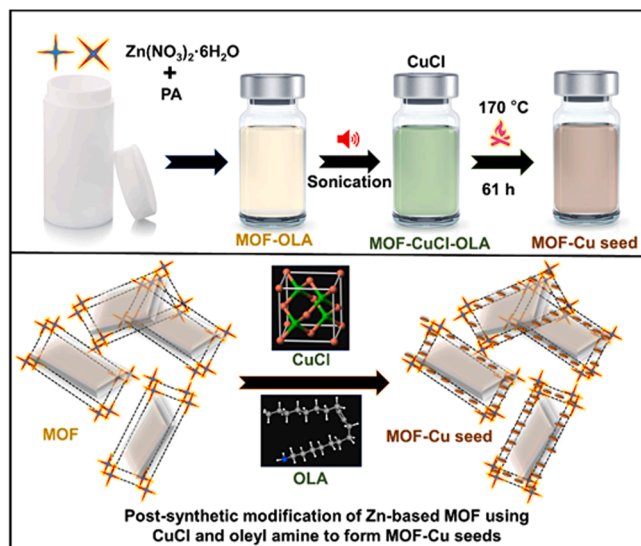
Fig. 1. Morphological characterization. (a, b) SEM images of MOF and (c, d) SEM images of MOF-Cu.

characterized by an average width and height of approximately 1.5 μm . Likewise, seed-enveloped surface morphology was unveiled for the MOF-Cu composite prepared from the MOF, CuCl, and OLA reaction mixture at 170 °C for 61 h (Fig. 1 (c and d)). SEM images exhibited the morphological evolution of the smooth MOF exterior to the copper seed-enveloped surface, with Cu seeds having a size less than 25 nm. Furthermore, the elemental composition through the EDAX spectrum confirmed the presence of Zn, C, N, and O in MOF and an extra Cu in the MOF-Cu seed composite (Fig. S2). The atomic percentages of Zn, C, N, and O in MOF are 14.29, 43.37, 4.32, and 38.02%, respectively. Whereas, in the MOF-Cu, atomic percentages of Zn, C, N, O, and Cu were around 24.9, 49.25, 0.58, 24.03, and 1.24%, respectively. Tables S1 and S2 display the elemental mapping of MOF and MOF-Cu, confirming the presence and distribution of the above-mentioned elements. However, the absence of other elements in the prepared materials confirmed the purity of MOF and MOF-Cu seed.

To study the crystalline growth of both the MOF and MOF-Cu seed composites, the samples were subjected to XRD (X-ray diffraction) analysis. Fig. 2a displays the diffraction pattern of MOF, proving the monoclinic crystal system, which agrees with the previous report by Zhong et al. Two Zn^{2+} ions can be crystallographically coordinated to a single water molecule, in addition to establishing bonds with five oxygen atoms derived from five carboxylate groups [17]. Fig. 2b shows the XRD data of the MOF-Cu, indicating a peak around $2\theta = 40^\circ$, which can be attributed to copper seeds in the prepared MOF [18]. Likewise, the detained peak response of MOF-Cu confirmed the sustained MOF structure after the copper seed enveloped. We analyzed the XRD data of Cu prepared from the CuCl-OLA mixture, as reported in previous studies [19] (Fig. S3). In this preparation mode, OLA functioned as a capping agent and as a solvent, reducing Cu^+ to Cu^0 [16]. As the reaction proceeded at room temperature, at 100 °C Cu^+ was reduced to Cu^0 , giving a grape wine color to the entire reaction mixture. At 170 °C, the generated Cu atom was recrystallized on the MOF surface as seed form via the Ostwald ripening mechanism [20,21].

3.2. Mode of bonding in the prepared MOF and MOF-Cu composite

Synthesized materials were analyzed in FT-IR to elucidate their bonding (Fig. 2c). The coordination of the Zn-O bond was confirmed by the presence of a stretching vibration peak at 517 cm^{-1} . Additionally, the absorption peaks at 1601 and 1379 cm^{-1} can be attributed to the stretching vibration of the carboxyl groups, while the peak at 697 cm^{-1} corresponds to the bending vibration of the C = O bonds. The broad absorption peak at 3426 cm^{-1} indicated the O-H stretching vibration, and the peak at 1601 cm^{-1} represents the deformation vibration of



Scheme 1. Schematic illustration for the preparation method of Zn-based MOF and MOF-Cu, and its post-synthesis modification of MOF to MOF-Cu seed.

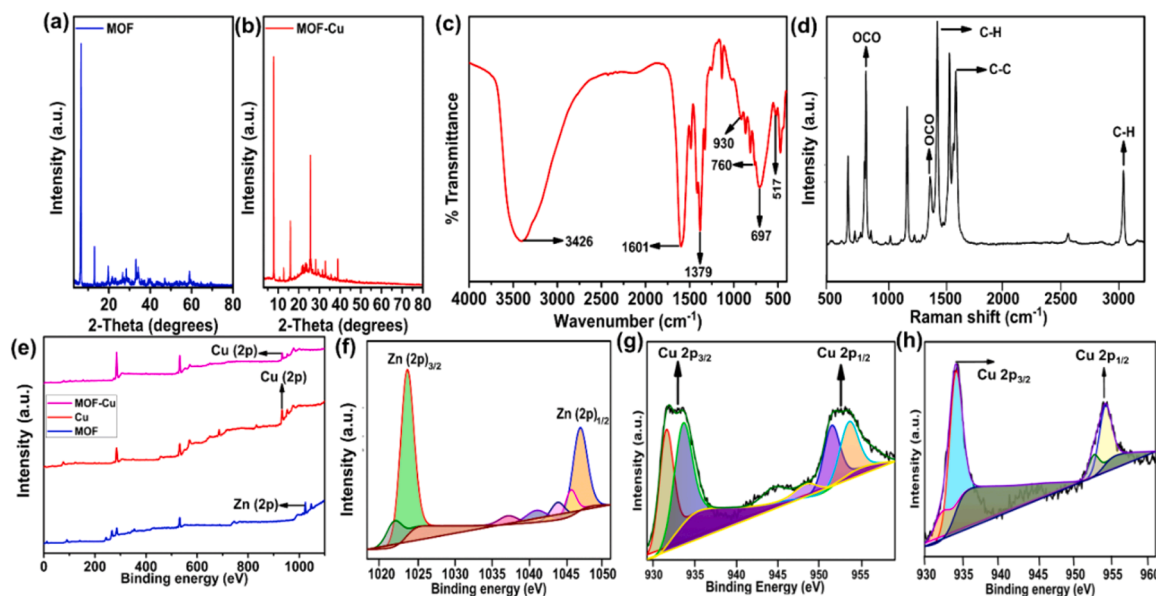


Fig. 2. (a, b) XRD patterns of MOF and MOF-Cu, (c) FT-IR spectrum of MOF, (d) Raman spectral plot for MOF, (e) XPS total survey spectrum of MOF, Cu, and MOF-Cu, (f-h) deconvolution spectrum of Zn in MOF, deconvolution spectrum of Cu from Cu-OLA mixture, and deconvolution spectrum of Cu in MOF-Cu.

water. Moreover, several absorption peaks were observed in the range between 930 cm^{-1} and 760 cm^{-1} , which further confirms the coordination between water molecules. Whereas Cu content had virtually no effect on the atomic vibration and surface functional group, providing a consistent peak for the MOF and MOF-Cu composite [22] (Fig. S4). Likewise, Fig. 2d displays the Raman spectra of the MOF. The sharp peak at 835 cm^{-1} and the weaker peak at 1394 cm^{-1} correspond to the scissoring and stretching of the OCO bond, respectively, in the MOF. Additionally, the absorption peaks at 1461 and 1610 cm^{-1} are linked to the in-plane C-H bending and C-C stretching of the benzene ring within the MOF structure. The presence of a sharp peak at 3070.5 cm^{-1} indicates the aromatic C-H stretching of the PA in the MOF. These sharp peaks confirm the crystalline nature of the MOF.

XPS spectra were used to characterize the bonding behavior of the synthesized materials. Fig. 2e illustrates the total survey spectra of MOF, Cu-OLA, and MOF-Cu, respectively. The presence of Zn (2p) (1022 eV) and Cu (2p) (933 eV) peaks in the distinctly prepared MOF and Cu-OLA confirms the formation of Zn-based MOF and copper nanoseeds. Whereas, the complete enveloping of Cu-seeds around the MOF gives a peak only for Cu at 933 eV , confirming the Cu^0 oxidation state in MOF-Cu. In detail, the deconvoluted spectrum of Zn-MOF gives two peaks at 1045 and 1022 eV , corresponding to Zn $2p_{1/2}$ and Zn $2p_{3/2}$ (Fig. 2f). Again, the high-resolution spectra for Cu prepared from the OLA mixture displayed two peaks at 952 and 932 eV , proving the presence of Cu $2p_{1/2}$ and Cu $2p_{3/2}$ spin states [23] (Fig. 2g). Based on the SEM data, Cu is uniformly distributed on the outer surface of the MOF after the Cu incorporation in the OLA mixture. As such, a similar binding energy for Cu from the prepared MOF-Cu composite indicates that the metal retained its Cu^0 oxidation state after incorporation (Fig. 2h). Thus, the XPS technique confirms the synthesis of a Zn-based MOF copper seed composite, verifying that Cu is in a zero-oxidation state.

3.3. The electrochemical response of MOF-Cu towards $[\text{Ru}(\text{NH}_3)_6]^{3+}$ in PBS

Positively charged ruthenium hexamine chloride ($[\text{Ru}(\text{NH}_3)_6]^{3+}$) (1 mM , $\text{pH} = 7.4$) was selected for the reversible single electron transfer kinetic studies in PBS [24]. The redox behavior of the MOF-Cu-GCE was characterized at potentials ranging from $+0.4\text{ V}$ to various cathodic potentials (-0.2 to -0.8 V) (Fig. S5a). Facile reduction of $[\text{Ru}(\text{NH}_3)_6]^{3+}$

to $[\text{Ru}(\text{NH}_3)_6]^{2+}$ was reversible at E_0 approximately -0.21 V . In addition, we studied the scan rate effect on the $[\text{Ru}(\text{NH}_3)_6]^{3+}$ (Fig. 3a). The $\log(\text{scan rate})$ vs. $\log(A)$ is in a good relationship for anodic current ($R^2 = 0.9666$). Based on Fig. S5b, where the slope is 0.09 , it is clear that the adsorption mechanism dominates in the reversible single electron transfer kinetics [25,26]. Negatively charged $\text{Fe}(\text{CN})_6^{3-/4-}$ (1 mM) was selected for the redox transfer kinetic studies in PBS. The MOF-Cu-GCE response was characterized by potentials ranging from -0.6 to $+0.6\text{ V}$ (Fig. 3b). The reduction peak for the ferricyanide to ferrocyanide is observed at -0.033 V . The decrease in current peak intensity with an increasing scan rate is attributed to the influence of adsorption of the analyte on the MOF-Cu-GCE. The $\log(\text{scan rate})$ vs. $\log(A)$ is in a good relationship for anodic current ($R^2 = 0.9948$). Based on Fig. S5d, where the slope is 0.3427 confirms that the adsorption dominates in the sensing mechanism. Charge transfer resistance (R_{ct}) is the measure of the strain in the transfer of an electron from one atom to another which is equivalent to the electrical resistance. In the case of a three-electrode system, R_{ct} is associated with the resistance between the electrode and electrolyte interface. From the Nyquist plot, the R_{ct} value was estimated to be 469.25 , 463.91 , and $372.6\ \Omega$ for MOF-GCE, bare GCE, and MOF-Cu-GCE (Fig. 3b) respectively. The lower R_{ct} value for MOF-Cu-GCE confirms the facile interfacial electron transfer between the catalyst and electrolyte interface [24]. Double layer capacitance (C_{dl}) measures the ability of an electrode-electrolyte interface to store the charge, often expressed in F/cm^2 . At this interface electric charges of opposing polarity form, one at the surface of the electrode (Helmholtz layer) and the other at the electrolyte (diffused layer). The single layer of solvent in between the Helmholtz and diffused layer will act like a dielectric. The C_{dl} value of the MOF-Cu-GCE towards DA sensing was estimated from the slope of scan rate vs. peak current plot, which is calculated to be $1.44\ \mu\text{F}/\text{cm}^2$ (Fig. S6).

3.4. The electrochemical response of MOF-Cu towards DA in HSA and PBS

A capacitive current CV plot is observed for bare GCE and MOF-Cu-GCE in the PBS (1 mM) (Fig. S7a). Through potential sweep, DA can undergo a redox reaction to form DA-quinone (DA-Q) [27]. In the presence of DA (200 nM , 1 mM PBS), bare GCE, Cu-GCE, and MOF-GCE show insensitive behavior towards the analyte in CV and DPV analysis

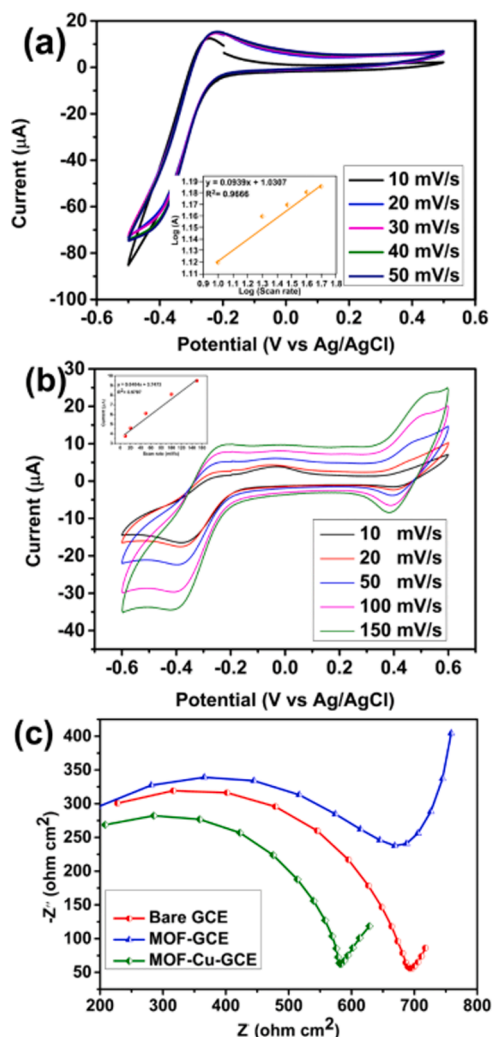


Fig. 3. (a) The scan rate effect on the [Ru(NH3)6]3+ in PBS and (b) The scan rate effect on the Fe(CN)6 3-/4- in PBS (c) Nyquist plot for different modified GCE in PBS.

(Fig. 4a and b). Whereas, an oxidation peak around 8.7 and 6.5 μA was observed in the MOF-Cu-GCEs CV and DPV plots. Therefore, MOF-Cu-GCE shows better sensitivity than other modified GCEs owing to favorable surface adsorption and fewer crystal defects due to Cu incorporation. Moreover, for a detailed study, we electrodeposited Cu on the MOF-GCE (Cu/MOF-GCE) using CV [28]. The DPV plot shows an insensitive behavior of Cu/MOF-GCE towards DA (Fig. S7b). Whereas, the DPV result from MOF-Cu-GCE supports that the DA oxidation peak increased linearly according to its concentration (50–1100 nM, 1 mM PBS-HSA), from a sensitivity of 5.58 to 11.23 μA.μM ($R^2 = 0.9975$) (Fig. 5 & S8). The limit of detection (LOD) was calculated as 9.28 nM based on the standard deviation (S_y) and slope (S) formulas as follows:

$$LOD = 3.3 \frac{S_y}{S} \quad (\text{Eq. 1})$$

So, MOF-Cu-GCE has a much better current response than other modified GCE because it selectively adsorbs DA, allows for better charge transfer, and provides a good environment for DA oxidation. Also, based on the results, we compared our MOF-Cu-GCE with other modified GCEs confirming the superiority of our material (Table 1) [29–34].

The scan rate gives the fluctuation of electric potentials with time. The redox behavior of 200 nM DA in 1 mM PBS (7.4 pH) was evaluated by sweeping the voltage from 10 to 50 mV/s (Fig. S9a). Results prove that the high scan influences the anodic current and gives a slight shift

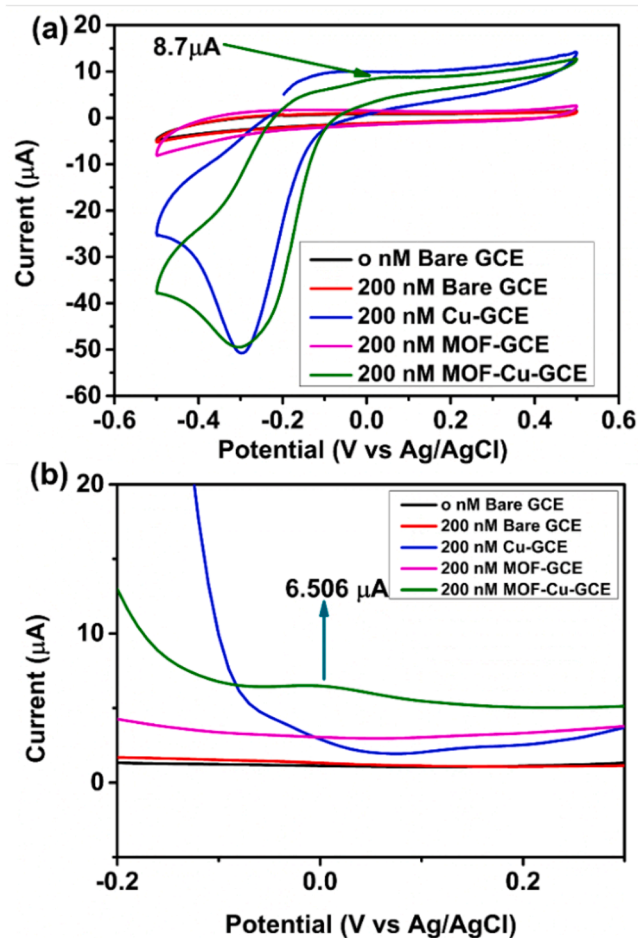


Fig. 4. (a, b) CV and DPV response of various modified GCE in HSA-PBS.

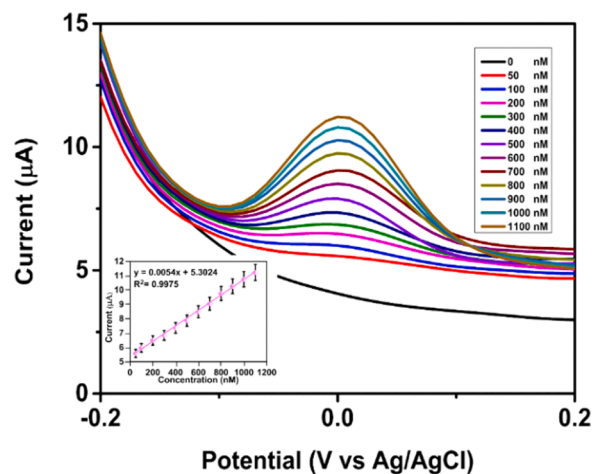


Fig. 5. DPV response of MOF-Cu-GCE towards DA in HSA-PBS.

for peaks due to the smaller diffusion layer [35–37]. Similarly, the kinetic behavior of the MOF-Cu-GCE was studied through the Log(A) vs. Log (scan rate) plot. Fig. S8b proves that the Log(A) and Log (scan rate) follow the linear equation;

$$y = 0.503x + 0.1236 \quad (\text{Eq. 2})$$

It is evident from the plot where the slope is 0.503 that adsorption predominates in the DA sensing mechanism by using MOF-Cu-GCE [38,

Table 1

Comparison of MOF-Cu-GCE with other modified GCEs.

Material	Technique	Linear range (μM)	LOD (μM)	Refs.
MOF-525-PEDOT NTs	DPV	2–270	0.04	[29]
Ce-MOF-808	AMP	20–200	1.3	[30]
Au@ZIF-8	DPV	0.1–50	0.01	[31]
SO ₃ -MOF-808/GO	DPV	50–500	2.3	[32]
Cu-Co(2-MeIm)	DPV	5.0–800	44.2	[33]
MOF@CNF//GCE				
HKUST-1/GCE	DPV	12.5–175	0.11	[34]
Zn-based MOF-Cu seeds	DPV	0.05–1.1	0.00928	This work

25].

The normalized current density (j_{norm}) for electrochemically active surface area (ECSA) compares the active surface area of a bare or modified electrode with different surfaces. The formula for j_{norm} is

$$j_{norm} = \frac{j}{ECSA} \quad (3)$$

j_{norm} is the normalized current density, j is the measured current density and ECSA is the electrochemically active surface area.

ECSA is the surface of the electrode which actively participates in the redox reaction. ECSA is the ratio of double-layer capacitance (Cdl) to the specific capacitance (C_s) which mathematically denotes as

$$ECSA = Cdl/C_s \quad (4)$$

Cdl is calculated from the slope of current density vs. scan rate plot (Fig. S6)

The specific capacitance (C_s) was calculated from the equation

$$C_s = \frac{\text{Area}}{\Delta E \times \text{scan rate} \times \text{voltage window} \times \text{mass}} \quad (5)$$

The area corresponds to the area under the CV curve, the scan rate in V/s, the voltage window is the difference between the highest and lowest potential, and mass corresponds to the weight of the sample in grams.

From the above data, we calculated the C_s as 0.937 F, ECSA as 15,368 cm²/g, and j_{norm} as 0.87 μA/g.

The protons have a significant effect on the sensing mechanism. The peak response of the MOF-Cu-GCE towards DA (200 nM) was observed at various pH values from 7.8 to 3.3 in PBS (1 mM). Fig. S10a and b displays the peak current increasing for pH values up to 6.4 due to selective adsorption through π - π interaction between DA and MOF-Cu [39, 40]. Conversely, deprotonation of DA will be weak in extremely acidic environments, leading to a drop in peak current.

3.5. MOF-Cu-GCE electrode selectivity study towards DA over EP and NE

EP and NE are two of the main interferants that curtail the detection of DA in voltammetry. As is well known, both DA, EP, and NE consist of a catechol unit that differs structurally only in their amine chain [8]. Therefore, the oxidation of catechol to quinone forms occurs simultaneously with DA, EP, and NE. To overcome this dilemma, the best strategy is to selectively adsorb DA on the modified GCE. Structurally, DA consists of a primary aminoethyl, whereas EP and NE contain beta-hydroxy secondary and primary amine chains [8]. From this, the EP and NE are more sterically hindered than DA for adsorption on suitable GCE surfaces. Similarly, DA is a weaker Lewis base than EP due to its primary and secondary amine chains [41–43]. Our group prepared Cu⁰ incorporated Zn-MOF to increase the electrical conductivity. The soft-soft interaction between Cu⁰ and DA gives selective sensing of DA over EP and NE [44–46]. The electrochemical sensing mechanism of the proposed MOF-Cu-GCE was demonstrated by depicting molecular structures (Fig. 6). The slope Eq. (2) from Log(A) and Log (scan rate) is 0.503, confirming that adsorption predominates in the DA sensing mechanism

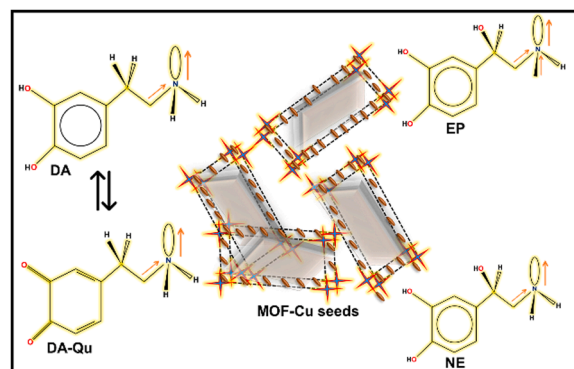


Fig. 6. Schematic representation for the selective electrochemical detection of DA over EP and NE.

of MOF-Cu-GCE (Fig. S8b). Based on the above theoretical background, we obtained a similar DPV result for DA sensing over EP and NE. From Fig. 7 and S11, MOF-Cu-GCE expresses an insensitive behavior in the presence of EP and NE (100 nM) in the HSA-PBS solution. Similarly, a sensitive behavior was obtained from MOF-Cu-GCE when DA (100 nM) was added to the same solution. We similarly repeated the experiment up to 500 nM, and the results verified the selective sensing of DA over NE and EP (Figs. S11 and 12).

3.6. MOF-Cu-GCE electrode selectivity study towards other interferants

Fig. S13a displays the interference response of various amino acids towards the MOF-Cu-GCE probe. DPV results confirm the insensitive behavior of 100 nM of each AC, CA, L-Cys, GABA, Glu, L-Glu, and L-His towards MOF-Cu-GCE. Likewise, cationic and anionic salts such as Na⁺, K⁺, Mg²⁺, PO₄³⁻, NO₃⁻, SO₄²⁻, and Cl⁻ exhibited a sustained current response before and after the addition of interferants (Fig. S13b). Thus, the DPV studies confirm the stability and sensitive nature of the prepared MOF-Cu-GCE.

3.7. Reproducibility, stability and real sample analysis using MOF-Cu-GCE

The stability and reproducibility of the modified GCE are pivotal in practical applications. The stability of the MOF-Cu-GCE was analyzed using DPV by repeating the experiment at a fixed concentration of DA (200 nM, HSA-PBS). Upon deducing the data, the obtained DPV result had a detained current response (Figs. 8a and S14a). From the data, we calculated the average and relative standard deviation (RSD) as 11.48

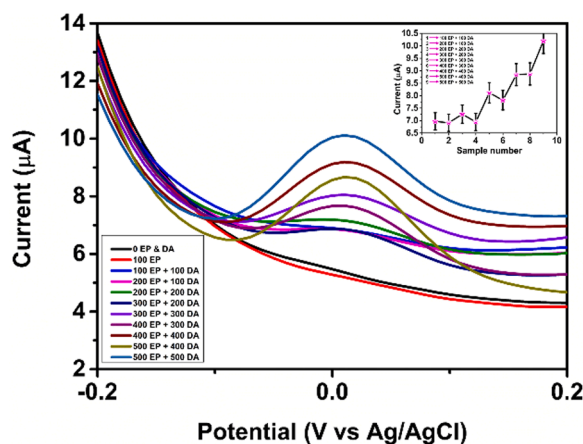


Fig. 7. Interference response of EP (0, 100, 200, 300, 400, and 500 nM) and DA (0, 100, 200, 300, 400, and 500 nM) towards MOF-Cu-GCE in HSA-PBS.

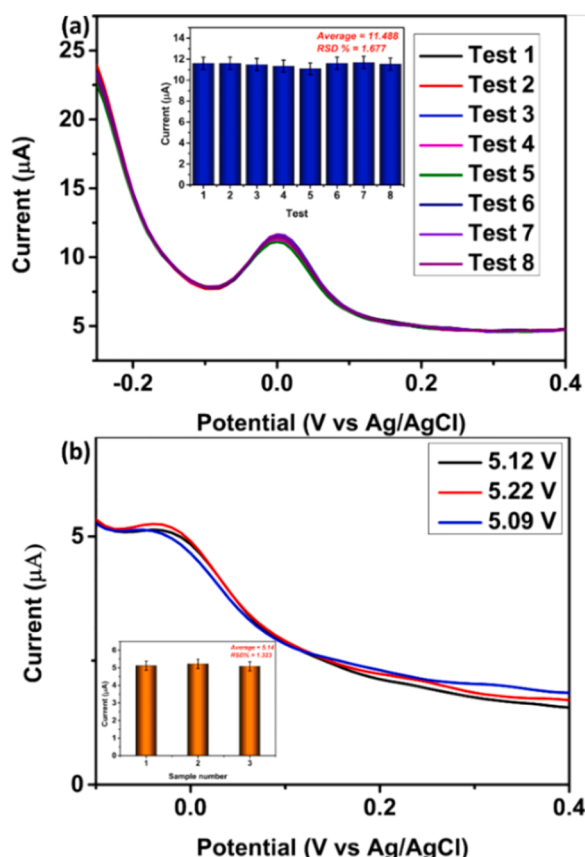


Fig. 8. (a and b) Stability and reproducibility DPV response of MOF-Cu-GCE in HSA-PBS.

and 1.67%, respectively ($n = 8$). Following five DPV tests, we conducted morphological and compositional studies on MOF-Cu. SEM-EDX analysis yielded results consistent with prior data, confirming the material's stability and un-leachable property of the prepared MOF-Cu (Fig. S15a and Table S3). Furthermore, the FT-IR results align with previous findings, affirming the stability of the bonding after the sensing (Fig. S15b). Similarly, the reproducibility of the MOF-Cu-GCE was tested by preparing the material three times and measuring its DPV response towards DA (100 nM) (Figs. 8b and S14b). The identical peaks observed in the DPV plot confirm the reproducibility of the work. Likewise, we calculated the average and RSD as 5.14 and 1.323%, respectively. We investigated the storage stability of the composite material. Specifically, we utilized a 10 μ l Nafion containing ethanol-dispersed MOF-Cu (0.5 mg in 1 ml), which was stored at -8°C for approximately 40 days. Differential Pulse Voltammetry analysis revealed the composite's insensitivity to a 50 nM dopamine solution. The incorporated Cu seeds on the surface were disrupted, possibly undergoing oxidation to their oxide form. We performed the real sample analysis using a mixture of human urine, HSA, and PBS. To prepare the human urine-HSA-PBS mixture, 10 mg of HSA was dissolved in a solution containing 10 ml of human urine and 10 ml of 1 mM PBS. The total volume was adjusted to 100 ml. The MOF-Cu-GCE system exhibited a response to DA within the concentration range of 50–500 nM in a human urine-HAS-PBS mixture (Fig. S16 a-c). The observed higher peak current intensity in the DPV plot for the HAS-PBS mixture compared to the urine-HAS-PBS solution can be attributed to the presence of dissolved ions and organic moieties. The ions and organic substances in the solvent significantly impact the electrochemical response.

4. Conclusions

In this work, our group employs a preparation scheme that offers an enhanced method for rectifying defects in the crystal phase of Zn-MOF using Cu^0 seeds, thus improving the electrochemical selectivity towards DA. For further studies, $[\text{Ru}(\text{NH}_3)_6]^{3+}$ and DA were used for the electrochemical characterization of the prepared MOF-Cu-GCE. This work testified that DA sensing is induced by the adsorption of an analyte on the MOF-Cu-GCE surface through soft-soft interaction and aromatic functionality. In addition, steric hindrance and the Lewis basic character of DA induce a selective sensing property towards MOF-Cu-GCE. Thus, the peak current was linearly proportional to DA from 50 to 1100 nM, and the LOD was found to be 9.28 nM ($R^2 = 0.9975$). Furthermore, experiments show the insensitive behavior of EP, NE, and other interferents towards MOF-Cu-GCE in the presence of DA. These findings indicate that the MOF-Cu-GCE demonstrates exceptional selectivity, sensitivity, stability, and reproducibility in detecting DA.

CRediT authorship contribution statement

Jose Paul: Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Roop-kumar Sangubotla:** Conceptualization, Methodology, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Jongsung Kim:** Supervision, Resources, Writing – review & editing, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.electacta.2024.143885](https://doi.org/10.1016/j.electacta.2024.143885).

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