



Electrochemical sensing of acetaminophen in biofluids, pharmaceutical and environmental samples using cobalt hexacyanoferrate decorated iron terephthalate metal organic framework

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ABSTRACT

Herein, a highly sensitive, cost-effective, and sustainable electrochemical sensor was developed for the selective sensing of acetaminophen (ACP) in actual samples using cobalt hexacyanoferrate (CHCF) incorporated iron terephthalate metal organic framework (FMF). The CHCF-FMF was sustainably synthesized and characterized using FTIR, XRD and SEM with EDX analysis. Using CHCF-FMF, a modified electrode was fabricated by drop-casting it over a glassy carbon, which on voltammetric investigations, revealed the presence of $\text{Co}^{2+/3+}$ redox couple with a formal potential of 0.51 V. Further, the designed sensor was employed for the electrocatalytic oxidation of ACP, which showed a linear detection range from 0.05 to 7.37 mM with a sensitivity and detection limit of 100.64 $\mu\text{A}/\text{mM}/\text{cm}^2$ and 13 μM , respectively. Furthermore, the developed CHCF-FMF/GCE sensing system is highly facile and robust, and it has demonstrated excellent stability, selectivity, repeatability, and good reproducibility. The superior performance was attributed to the *in-situ* formation of CHCF over FMF, which efficiently arranged them to augment the electrochemical and electrocatalytic properties. Besides, the sensor was employed to determine ACP in blood serum, commercial tablets, and environmental samples, which showed recovery ranges of 96.2% – 106.2%. This work provides a novel strategy for designing catalytically active sites at the molecular level, which opens a new avenue in fine-tuning MOFs for their applicability in medical diagnostics, point-of-care, industrial and environmental monitoring devices.

1. Introduction

The selective detection of acetaminophen (ACP) in biofluids, pharmaceutical and environmental samples is imperative owing to their inimical effects on human and animal health [1–3]. ACP (commonly Paracetamol, Tylenol, Panadol, etc.) is a non-steroidal anti-inflammatory drug (NSAID) with antipyretic and analgesic effects. ACP and other NSAID drugs are consumed by most of the population (>30 million daily users) to treat common flu, cold, headache, muscle aches, toothaches, body pain, arthritis and so forth [4,5]. Also, ACPs are used in combination with other drugs and as a result, every year >100,000 metric tons of ACPs are manufactured and consumed worldwide in their direct or combined form [6]. However, this crowning drug has evil effects when it is taken more than the allowed limit. Overconsumption of ACPs causes various diseases and disorders, starting from insomnia, nausea, seizures, trembling, and ulcers to life-threatening conditions like renal failure, heart attack and fulminant hepatic necrosis [7,8]. On the

other hand, ACP is a subclass of organic contaminants and is also considered an emerging chemical pollutant in aquatic and other natural environments. Furthermore, ACPs are found in wastewater treatment plants and open water bodies in the United States, United Kingdom, and other countries [9]. ACP enters the soil and water bodies through various sources, including clinical disposal, consumer excretion, pharmaceutical effluents, unconsumed or expired drug disposals, etc. [10–12]. Besides, chronic exposure would result in cancer, drug resistance, endocrine disruption, inhibition of cell proliferation and several other chronic diseases [13]. Therefore, developing simple, highly sensitive, economically viable, exceedingly responsive, and accurately determining methodologies for ACP detection is highly demanding in clinical, industrial, and environmental monitoring.

Among various methods used to determine ACP (including titrimetry, high-performance liquid chromatography, capillary electrophoresis, spectrofluorimetric, spectrophotometry, chemiluminescence, and liquid chromatography combined mass spectrometry), electrochemical

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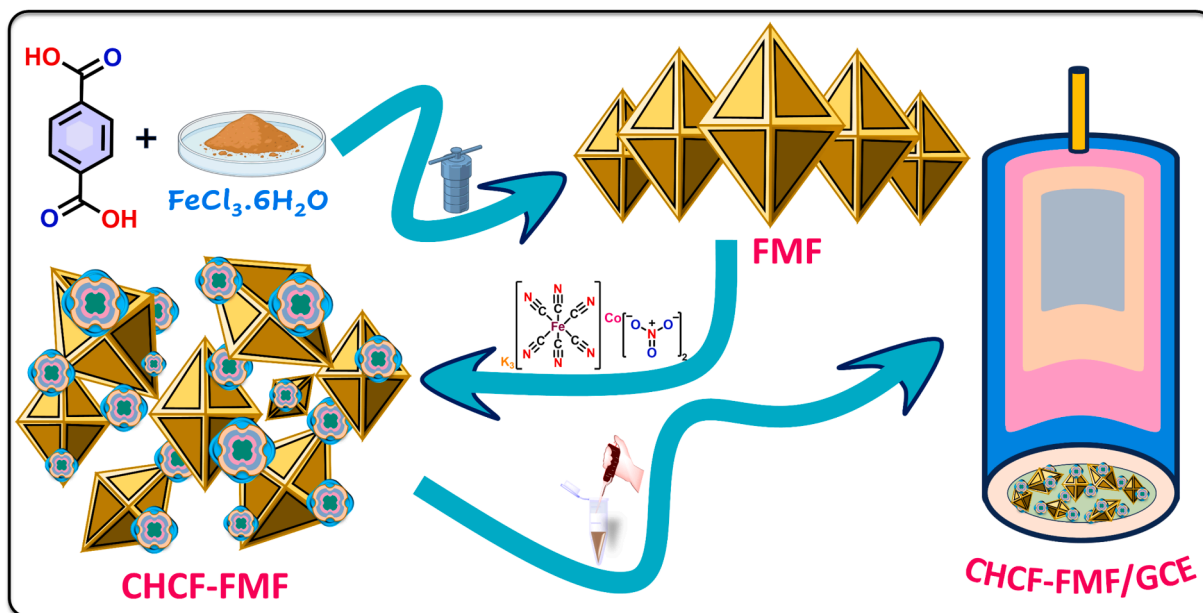


Fig. 1. Graphical illustration for the synthesis of CHCF-FMF and fabrication of CHCF-FMF/GCE.

methods are highly preferred due to many of the following reasons [14–16]. Electrochemical sensors (ECS) are superior technologies that detect or quantify the target analytes at their trace levels in a fraction of time. Moreover, ECS are facile, cost-effective, rapidly responsive, highly selective, and sensitive, simple to operate, portable, can be miniaturized and require less sample volume [17–19]. Hence, ECS is one of the most preferred methodologies for detecting ACPs and other trace analytes. A bimetallic MOF (Fe-Mg) anchored black phosphorous nanosheets modified GCE showed responses for ACP along with ascorbic acid, uric acid, and dopamine [20]. Similarly, MOF-derived Ni-doped porous carbon spheres modified GCE displayed responses for ACP along with uric acid and dopamine [21]. A polyglycine modified GCE was utilized for ACP detection in children's syrup, whose performance was affected in the presence of a 10-fold concentration of caffeine [22]. Therefore, detection of ACP via electrooxidation often interferes with other easily oxidizing molecules such as dopamine, ascorbic acid, uric acid, etc. Hence, designing a selective and sensitive electrocatalyst for ACP is the most challenging part of the ECS construction [23,24].

To address this, various electrocatalysts in combination with materials and molecules have been proposed for the selective sensing of ACPs, which includes ionic liquids, organic frameworks, 2D & 3D nanomaterials, metal nanoparticles, complexes and oxides, carbon nanomaterials, redox dyes, polymers, and other redox compounds [25–27]. Metal organic frameworks (MOFs) are porous organic-inorganic hybrid systems with a large surface area, customizable pore volumes, and abundant catalytically active sites with good electrochemical properties [28,29]. In addition, MOFs have various advantages, such as cost-effectiveness, ease of synthesis, and good scalability with synthetic and structural versatility. Moreover, MOFs are biocompatible, biodegradable and can be synthesized sustainably [30, 31]. Due to these reasons, MOFs are utilized in various fields such as catalysis, biomedical applications, gas storage and separation, energy harvesting and storage, electrochemical sensing, and so forth [20,32]. On the other hand, metal hexacyanoferrates (MHCFs) are a class of multi/mixed-valance compounds with unique physical and chemical properties [33]. Among various MHCFs, cobalt hexacyanoferrates (CHCFs) are well explored, and their redox properties have been known for decades. Besides, CHCFs are easy to synthesize, cost-effective, possess good ionic conductivity, biocompatibility, and excellent electrochemical and electrocatalytic activities [34–36]. Hence, they are

being utilized in various electrochemical applications, including supercapacitors, batteries, electrochemical sensors, and electrochromic devices [37,38]. Even though both MOFs and MHCFs have been known for decades and well explored individually for various applications, their combined activities have not been explored much, and hence, there are a whole lot of interesting opportunities available to explore in this direction.

With the above background, a robust ACP sensor was designed using cobalt hexacyanoferrate (CHCF) incorporated iron terephthalate metal organic framework (FMF) modified glassy carbon electrode (GCE). CHCF-FMF was synthesized using a sustainable process with less to non-hazardous reagents. The synthesized materials and the fabricated sensor were characterized by spectroscopical, morphological, elemental, and electrochemical techniques. The developed sensor showed excellent sensitivity and selectivity towards ACP oxidation. Moreover, the designed sensor is highly facile, economical, sustainably obtained, nontoxic, and has various other advantages, like good stability, reliable reproducibility, and acceptable repeatability. Further, it was employed for ACP sensing in biofluids, pharmaceutical formulations and environmental samples, which demonstrated excellent recoveries. The outstanding performance was attributed to the *in-situ* formation of CHCF within the FMF structure, which efficiently arranged them for advanced homogeneity and augmented electrochemical activity. This approach provides a facile strategy to improve the electrocatalytic activity of MOFs by tuning their structure at the molecular level, thus opening its applicability to next-generation sensing devices.

2. Experimental methods

2.1. Materials and instrumentation methods

Iron(III) chloride hexahydrate ($\geq 99\%$), cobalt(II) nitrate hexahydrate ($\geq 98\%$), acetaminophen ($\geq 99\%$), potassium hexacyanoferrate(II) trihydrate ($\geq 98.5\%$), L-ascorbic acid ($\geq 99\%$), dextrose, dopamine hydrochloride, β -NADH ($\geq 97\%$), human serum and rabbit serum were procured from Sigma Aldrich, Korea. Terephthalic acid ($>99\%$), potassium chloride ($>99.5\%$), potassium hexacyanoferrate(III) ($>98\%$), 2,2-bis(4-hydroxyphenyl)propane were received from Tokyo Chemical Industry, Korea. The commercial tablet was purchased from a local drugstore. Aqueous Ag/AgCl electrode and glassy carbon electrode

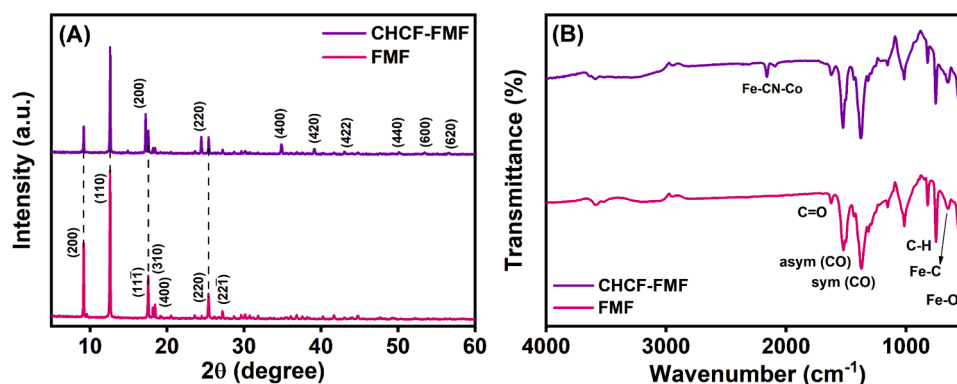


Fig. 2. (A) FTIR and (B) XRD analysis of FMF and CHCF-FMF.

(GCE) with a geometric area of 0.071 cm^2 were obtained from CH instruments, Austin and used as the reference (RE) and working electrode (WE), respectively. A platinum spiral electrode received from BASi, USA, was used as the counter electrode (CE). A JASCO FT/IR-4600 spectrometer was used to record the Fourier-transform infrared (FTIR) spectra, and a Rigaku ultima III X-ray diffractometer was used to analyze the powder X-ray diffraction (XRD) patterns of the synthesized samples. Hitachi SU8600 with a cold cathode field emission electron gun was used to acquire the scanning electron microscope (SEM) images. Cyclic voltammetry, differential pulse voltammetry and electrochemical impedance measurements were performed in IVIUM CompactStat.h potentiostat, Netherlands. Milli-Q water ($18.2 \text{ M}\Omega \text{ cm}$) from the Merck Millipore water system was used to make aqueous solutions. For practical sample analysis, the obtained serum and facet water samples were diluted 20 times with 0.1 M KCl solution, and a standard addition method was followed by spiking known concentrations of ACP. For commercial tablet analysis, the tablet was dissolved in 0.1 M KCl solution and centrifuged at 6000 rpm for 20 min . The obtained supernatant was made up to the mark in a standard 100 mL volumetric flask with 0.1 M KCl solution and used as the tablet stock solution.

2.2. Synthesis of FMF and CHCF-FMF

Fig. 1 briefly illustrates the synthesis of FMF, CHCF-FMF, and the electrochemical sensor CHCF-FMF/GCE fabrication. At first, the iron terephthalate metal organic framework (FMF) was synthesized by a solvothermal method, and then CHCF was formed *in-situ* in aqueous FMF at room temperature (RT) [39,40]. In a typical procedure, equimolar amounts of iron(III) chloride hexahydrate and terephthalic acid were dissolved in DMF separately and stirred until both dissolved. Afterwards, the terephthalic acid solution was slowly poured into the iron chloride solution and stirred continuously for 1 h . Next, the reactants were poured into a stainless-steel autoclave, then tightly sealed and kept in a hot air oven at 150°C for 15 h . After completion of the reaction, the autoclave was cooled to RT, and the solid residue was repeatedly centrifuged and washed with DMF, Milli-Q water and ethanol and the product was dried at 80°C for 12 h to obtain the FMF. Thereafter, 100 mg of the prepared FMF was added to a 500 mL beaker containing 200 mL of Milli-Q water and the solution was ultrasonicated for 90 min to obtain uniform dispersion. The obtained dispersion was constantly stirred at RT, to which 30 mL of aqueous cobalt(II) nitrate hexahydrate (10 mM) was added dropwise. After completion, the reaction mixture was continuously stirred for 2 h at RT. Subsequently, 20 mL of aqueous potassium hexacyanoferrate(III) (10 mM) was added drop by drop to the stirring reaction mixture. As the addition continues, the solution becomes turbid, which implies the formation of CHCF-FMF and after complete addition, the reaction mixture was continuously stirred for 24 h at RT. The solid product was separated by centrifugation and washed repeatedly with Milli-Q water and ethanol. Finally, dried in a vacuum

oven at 60°C for 12 h yields the CHCF-FMF.

2.3. Fabrication of CHCF-FMF/GCE

Before the fabrication of CHCF-FMF/GCE, the bare GCE was thoroughly mirror-polished with increasing grades of alumina slurries against the polishing pad. Then, the GCE was ultrasonically cleaned with ethanol and water (1:1) mixture for 2 min to remove the alumina and other foreign particles and then dried with a continuous stream of nitrogen. The CHCF-FMF ink was prepared by ultrasonating 5 mg of CHCF-FMF in $500 \mu\text{L}$ solvent mixture ($240 \mu\text{L}$ of Milli-Q water, $250 \mu\text{L}$ of ethanol and $10 \mu\text{L}$ of $5 \text{ wt\%}$ Nafion) for 6 h . From the stably dispersed CHCF-FMF ink, a portion of $3 \mu\text{L}$ (optimized) was pipetted over the precleaned GCE, and then dried in the room atmosphere for 90 min to obtain the CHCF-FMF/GCE sensor. By following the same protocol, FMF/GCE was fabricated for comparison. The fabricated sensors were stored in a closed, dry place for further studies.

3. Results and discussions

3.1. Material characterization

The synthesized FMF and CHCF-FMF were characterized by powder XRD, FTIR and SEM with EDX analysis. Fig. 2A displays the XRD pattern obtained for FMF and CHCF-FMF. In the XRD pattern of FMF, the diffraction peaks at 2θ values 9.21° , 12.59° , 17.59° , 18.14° , 18.45° , 25.39° and 27.24° were assigned to the planes 200, 110, $11\bar{1}$, 310, 400, 220, and $22\bar{1}$, respectively. These diffraction peaks are consistent with previous reports and demonstrate that FMF has been successfully prepared [41]. After the *in-situ* formation of CHCF in the presence of FMF, the XRD pattern of CHCF-FMF retains all the major peaks of FMF, along with new CHCF peaks. The new peaks at 2θ values 17.22° , 24.47° , 34.86° , 39.15° , 43.03° , 50.16° , 53.41° , and 56.72° in the CHCF-FMF were assigned to the planes 200, 220, 400, 420, 422, 440, 600, and 620, respectively which are consistent with previous CHCF reports [42]. Moreover, there were no shift in the positions of FMF characteristic peaks in CHCF-FMF, which indicates that the *in-situ* formation of CHCF did not alter FMF crystallinity. Moreover, the well-matched XRD pattern and intense sharp peaks confirm the formation of highly crystalline FMF and CHCF-FMF. To investigate the functional groups further, FTIR was performed and Fig. 2B depicts the FTIR comparison spectra of FMF and CHCF-FMF. In the FMF spectra, the bands at 1622 , 1523 , and 1369 cm^{-1} correspond to C=O stretching, asymmetric and symmetric stretching vibrations of dicarboxylate linker present in the FMF, respectively. Furthermore, the appearance of characteristic vibration bands at 648 and 517 cm^{-1} corresponding to Fe-C and Fe-O bonds confirm the formation of FMF [43]. After CHCF-FMF formation, all the vibration bands of FMF were retained along with new peaks corresponding to Fe-CN—Co stretching vibrations of CHCF appeared at 2158 and 2091 cm^{-1} , which

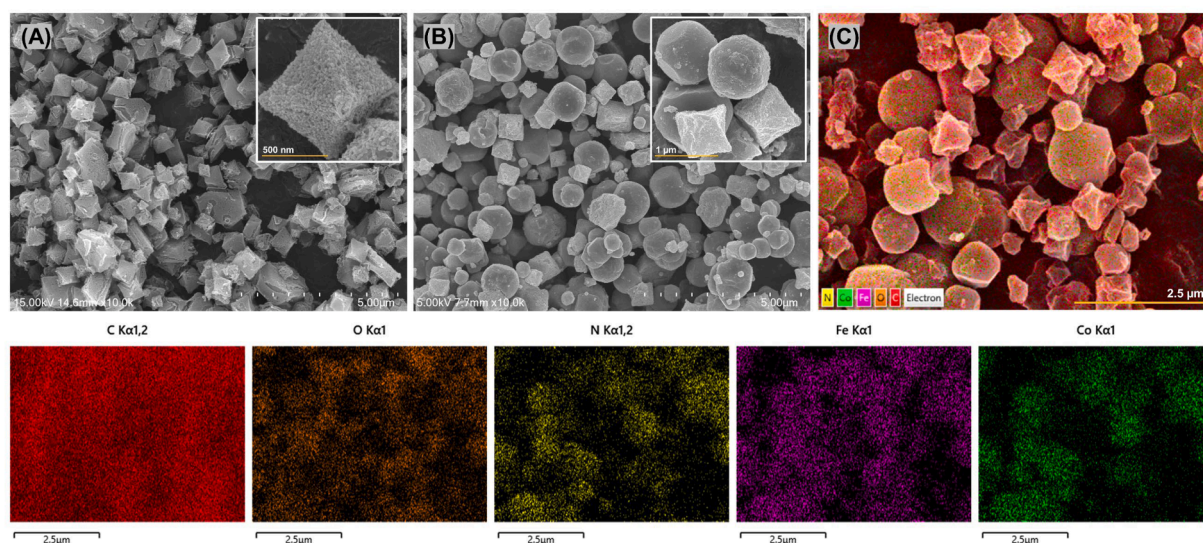


Fig. 3. (A) & (B) SEM of FMF and CHCF-FMF (Insets: selected area enlarged view of FMF and CHCF-FMF). (C) Overlaid and individual elemental mapping images of CHCF-FMF.

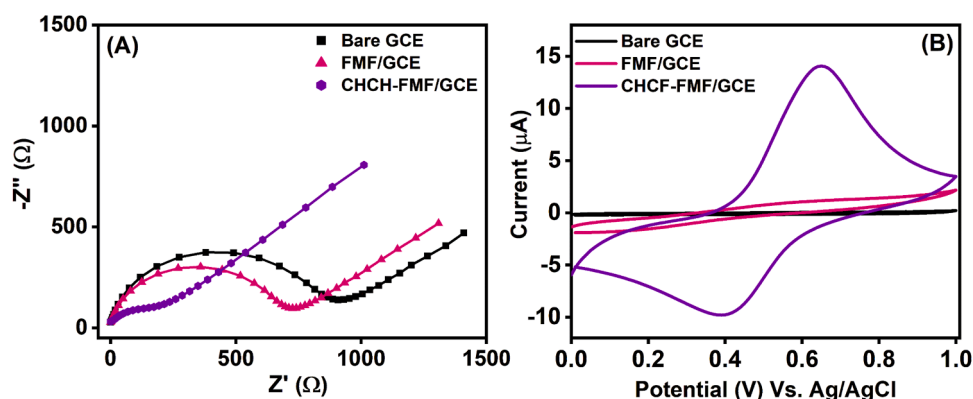


Fig. 4. (A) EIS spectra in 0.1 M KCl containing 5 mM of $[\text{Fe}(\text{CN})_6]^{3-/4-}$ and (B) CVs in 0.1 M KCl at 50 mV s^{-1} of Bare GCE (black), FMF/GCE (magenta) and CHCF-FMF/GCE (violet).

confirms the formation of CHCF in the FMF framework [44]. Also, there were no observable shifts in the peak positions of FMF, which again supports the XRD results that the incorporation of CHCF did not alter the nature and crystallinity of FMF.

SEM with EDX analysis was also performed to investigate the morphology and elemental composition of FMF and CHCF-FMF. In the SEM image of FMF (Fig. 3A), we could see the octahedron morphologies of FMF with a uniform grain diameter of $\sim 500 \text{ nm}$. Further, elemental mapping and composition (Fig. S1 & S2) confirm the presence of Fe, C and O in the FMF structure [45]. In the SEM of CHCF-FMF (Fig. 3B), we could see the appearance of well-dispersed truncated-sphere shaped CHCF within the octahedron FMF structures, which confirms the formation CHCF-FMF [46]. Besides, the *in-situ* formation of CHCF did not alter the structural morphology of the FMF. Further, elemental mapping (Fig. 3C) of CHCF-FMF shows the presence of well-dispersed Co, Fe, C, N and O elements, where Fe and Co species are uniformly distributed with almost equal atomic ratios (Fig. S3). In conclusion, XRD, FTIR and SEM with EDX analysis corroborates the successful formation and uniform distribution of FMF and CHCF-FMF and confirms that the incorporation of CHCF did not alter the FMF nature and morphology.

3.2. Electrochemical investigation

After successfully characterizing the synthesized FMF and CHCF-

FMF, the next step is to explore their electrochemical and electrocatalytic properties towards ACP. Before that, to attain the maximum performance of the proposed sensor, several fabrication conditions, such as the loading volume of the electrocatalyst (CHCF-FMF) and the drying time of the sensor, were optimized. As illustrated in Fig. S4 A&B, the maximum current responses were obtained when the loading volume and drying time were $3 \mu\text{L}$ and 90 min, respectively. These optimized conditions were followed to fabricate all CHCF-FMF/GCE used in this work. To begin with, electrochemical impedance spectroscopy (EIS) was performed with all the modified electrodes in 0.1 M KCl containing 5 mM of potassium ferricyanide and ferrocyanide and the obtained EIS data are shown in Fig. 4A. The EIS data has two regions, a semicircle part at higher frequencies and linear part at lower frequencies and the charge transfer resistance (R_{ct}) was obtained by measuring the diameter of the semicircle. In Fig. 4A, the black curve represents the EIS of bare GCE, which has a high R_{ct} of 906Ω , due to the sluggish electron transferability of bare GCE. After modifying the GCE with FMF (FMF/GCE, magenta curve), the R_{ct} value was slightly reduced to 725Ω , denoting the better electron transferability of FMF than bare GCE. Interestingly, after immobilizing CHCF-FMF (violet curve) on GCE, the R_{ct} value was further reduced to a low value of 181Ω , indicating the superior electron transferability of the proposed sensor. Next, cyclic voltammetry was performed with all the modified electrodes in 0.1 M KCl at 50 mV s^{-1} between the potential window 0 to 1.0 V, and the obtained cyclic

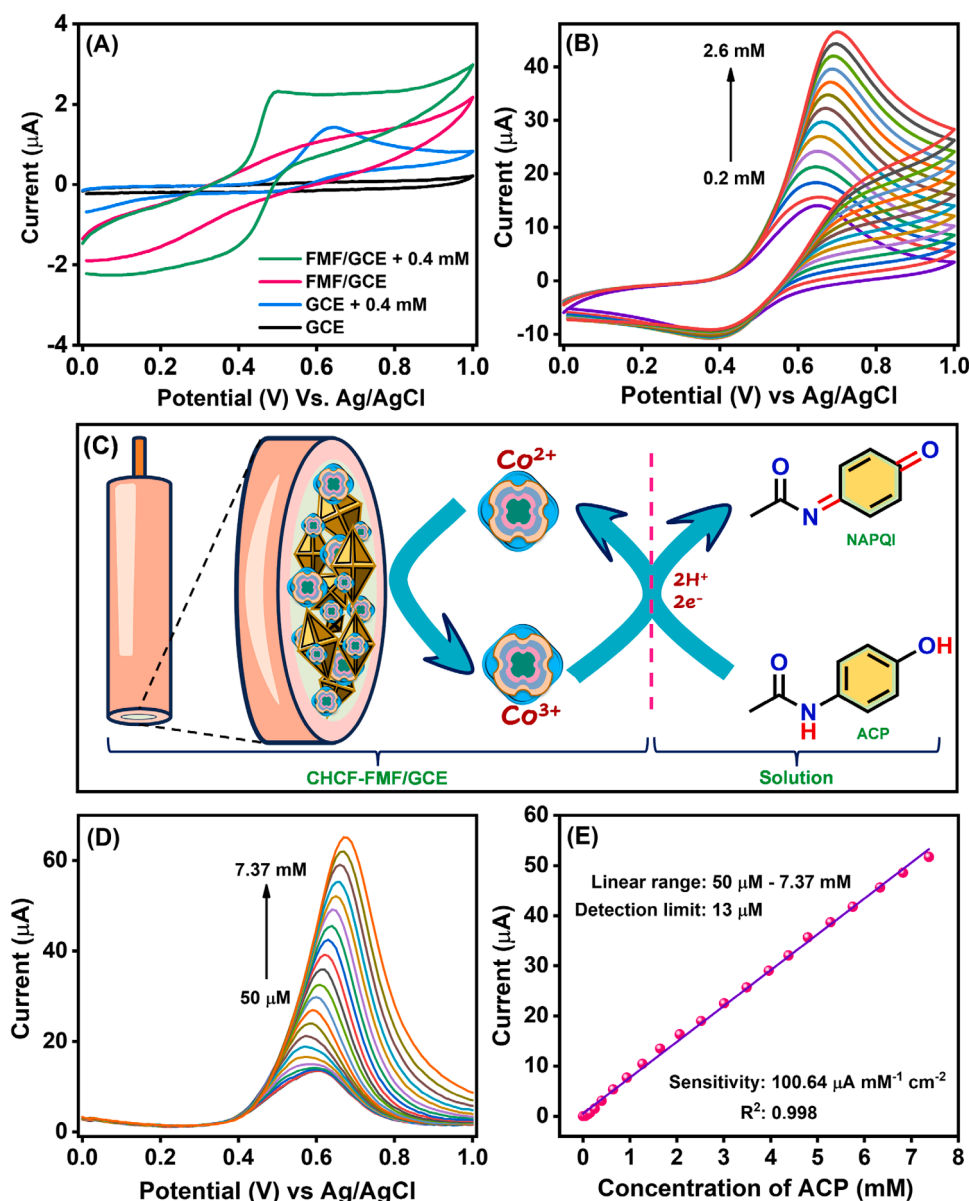


Fig. 5. (A) CVs of Bare GCE and FMF/GCE in the absence and presence of 0.4 mM ACP, (B) CVs of CHCF-FMF/GCE for the sequential additions of 0.2 mM ACP. (C) Mechanism for the electrocatalytic oxidation of ACP to NAPQI by CHCF-FMF/GCE. (D) DPVs of CHCF-FMF/GCE for the sequential additions of various concentrations of ACP and (E) its corresponding calibration plot. Electrolyte: 0.1 M KCl; Scan rate: 50 mV s⁻¹.

voltammograms (CVs) are shown in Fig. 4B. The CV of bare GCE (black curve) did not show any peaks, implies the absence of electroactive materials on the surface of bare GCE. After modifying the GCE with FMF, the FMF/GCE (magenta curve) showed a CV response slightly broader than bare GCE, implying the capacitive behavior of FMF. Interestingly, after incorporating CHCF in the FMF, the CHCF-FMF/GCE (violet curve) performance was significantly improved. It showed a well-defined redox peak at the formal potential (E^0) of 0.51 V, with anodic (E_{pa}) and cathodic peak potentials (E_{pc}) at +0.64 V and +0.39 V, respectively, corresponding to the Co^{2+/3+} redox couple present in the CHCF of CHCF-FMF [47]. The superior performance of the developed sensor could be due to the *in-situ* formation of CHCF, which stably arranges them over the FMF, thereby synergistically augmenting the electrochemical properties. Further, the effect of scan rate on CHCF-FMF/GCE was investigated by varying the scan rate from 10 to 200 mV s⁻¹ in 0.1 M KCl and the obtained voltammograms are depicted in Fig. S5A. While increasing the scan rates, both the peak currents were linearly increased with the scan rate and the plot of scan rate against peak currents yielded

a linear response, denoting the surface controlled redox process (Fig. S5B) at CHCF-FMF/GCE.

3.3. Electrocatalytic activities of CHCF-FMF/GCE towards ACP

The superior electrochemical properties of the proposed sensor inspired us to explore its electrocatalytic activity towards ACP. Accordingly, CVs were performed with various modified electrodes in 0.1 M KCl with different concentrations of ACP. Fig. 5A displays the CVs of bare GCE and FMF/GCE in the absence and presence of 0.4 mM ACP at 50 mV s⁻¹. For the oxidation of ACP, the bare GCE showed the onset at 0.5 V, while for FMF/GCE, the onset was decreased to 0.4 V, and it showed better sensitivity than bare GCE. After incorporating CHCF, the CHCF-FMF/GCE showed a better current response with improved sensitivity for every addition of 0.2 mM ACP, as portrayed in Fig. 5B. Moreover, CHCF-FMF/GCE showed ~2.5 and ~3.5-folds of excess electrocatalytic current response for ACP oxidation than FMF/GCE and bare GCE, respectively. Further, the electrocatalytic mechanism of

Table 1

Electrocatalytic performance comparison of CHCF-FMF/GCE with other sensors.

Electrocatalyst	Linear range	Detection limit (μM)	Sensitivity	Real samples	Ref.
NiCu-CAT/GCE	5 – 190 μM	5	$0.147 \mu\text{A} \mu\text{M}^{-1}$	Commercial tablets	[23]
GrRGC	0 – 50 μM	8.36	–	Tablets and synthetic urine	[49]
Polyimide-MWCNT/Pt	2 μM – 1.8 mM	2	$2.27 \mu\text{A} \text{mM}^{-1}$	Commercial tablets	[50]
Au-Ag/ITO	10 μM – 1 mM	2.4	–	Tablets and urine	[51]
AgD/GCE	2.5 μM – 10 mM	2.5	–	–	[52]
ZnO-MoO ₃ -C/GCE	2.5 μM – 2 mM	1.14	$18.5 \mu\text{A} \text{mM}^{-1}$	Serum and tablets	[53]
Recycled-rGO/GCE	60 – 500 μM	0.28	$83 \mu\text{A} \text{mM}^{-1}$	Commercial tablets	[54]
ZTODH/CPE	1 – 7 mM	–	–	–	[55]
CBZ/CPE	100 – 394 μM	0.24	–	Commercial tablets	[56]
La _{0.95} Co _{0.05} MnO ₃	1 – 5 mM	–	–	–	[57]
WO ₃ /GCE	75 μM – 6.75 mM	52.9	$43 \text{nA} \mu\text{M}^{-1} \text{cm}^{-2}$	Urine	[58]
β -CD/RGO/GCE	10 μM – 0.8 mM	2.3	$27.8 \mu\text{A} \text{mM}^{-1}$	–	[59]
Au/ZnO/N-Gr/GCE	5 μM – 3.1 mM	0.8	–	Serum and urine	[60]
NanoMIPs/SPCE	100 μM – 1 mM	50	–	Human plasma	[1]
Fe ₃ O ₄ -M221/GCE	50 μM – 2 mM	16	$7.46 \mu\text{A} \mu\text{M}^{-1} \text{cm}^{-2}$	Commercial tablets	[61]
AuNP-PGA/SWCNT	50 – 300 μM	15	$13.3 \mu\text{A} \text{mM}^{-1}$	Commercial tablets	[62]
CHCF-FMF/GCE	50 μM – 7.37 mM	13	$100.64 \mu\text{A} \text{mM}^{-1} \text{cm}^{-2}$	Serum, tablets, and environmental samples	This work

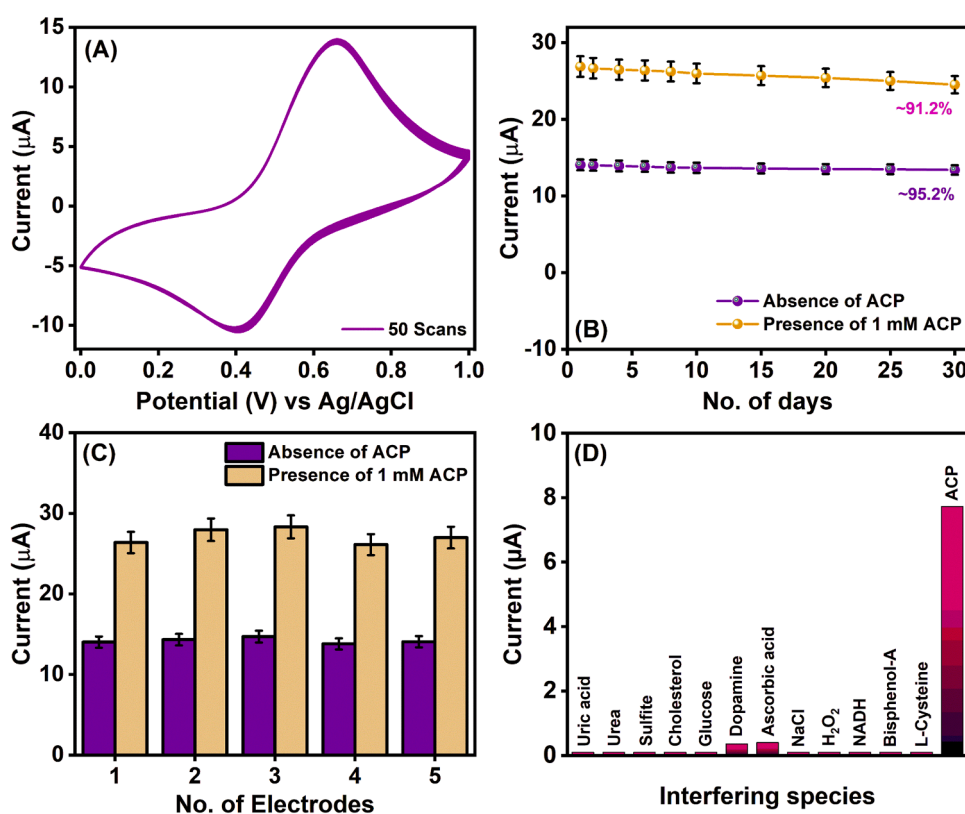


Fig. 6. (A) CVs of CHCF-FMF/GCE for 50 consecutive scans at 50 mV s^{-1} . CV current response of CHCF-FMF/GCE in the absence and presence of 1 mM of ACP (B) 30 days and (C) five different sensors. (D) Electrocatalytic current response (DPV) of CHCF-FMF/GCE for 1 mM ACP and 0.5 mM of various interfering species. Electrolyte: 0.1 M KCl.

CHCF-FMF/GCE could be explained as follows [48]. When the ACP was added, the oxidized CHCF-FMF (Co^{3+}) on the electrode oxidizes the ACP in the electrolyte solution to N-acetyl-p-quinone imine (NAPQI) and it gets reduced to CHCF-FMF (Co^{2+}) as shown in Fig. 5C. The reduced CHCF-FMF (Co^{2+}) gets re-oxidized at electrode and oxidizes the approaching ACPs and this process continues until all the ACPs are oxidized. Further, differential pulse voltammetry was performed with the developed sensor between the same potential window as that of CVs, to explore its linear detection range, the limit of detection (LOD), sensitivity and selectivity. The obtained differential pulse voltammograms (DPVs) are shown in Fig. 5D, and it is evident that for every addition of ACP, there was a linear increase in the oxidation current.

Fig. 5E shows the plot of catalytic current vs ACP concentration, and the linear detection range was calculated to be 50 μM to 7.37 mM ($R^2 = 0.998$) with a sensitivity and LOD of $100.64 \mu\text{A} \text{mM}^{-1} \text{cm}^{-2}$ and 13 μM ($S/N = 3$), respectively. It is apparent that CHCF-FMF/GCE displayed an improved current response with better sensitivity than FMF/GCE and bare GCE. The superior performance of CHCF-FMF/GCE could be attributed to the in situ formation of CHCF, which stably arranged them over the FMF, thereby synergistically enhancing the overall performance. Furthermore, the obtained performance of the proposed sensor towards ACP is compared with the recent literature, and the performances are comparable or better than the previous reports, as shown in Table 1.

Table 2
ACP determination in real samples.

Samples	Spiked (μM)	Found (μM)	Recovery (%)	%RSD ^a
Human Serum (HS)	200	196	98.0	3.6
	400	409	102.2	4.2
Rabbit Serum (RS)	200	211	105.5	2.9
	600	621	103.5	3.7
Facet water	500	531	106.2	3.8
	1000	972	97.2	4.2
	1500	1443	96.2	4.1
Commercial Tablet	500	524	104.8	3.6
	1000	976	97.6	3.8
	1500	1469	97.9	4.1

^a Triplicates.

3.4. Investigating the stability, reproducibility, and selectivity of CHCF-FMF/GCE towards ACP

It is a prerequisite to investigate the stability, reproducibility, and selectivity of the fabricated sensor. Initially, the stability of CHCF-FMF/GCE was examined by performing 50 continuous potential cycles in 0.1 M KCl at a scan rate of 50 mV s⁻¹. It is evident from Fig. 6A that the fabricated sensor is highly stable and did not undergo any noticeable change even after 50 continuous cycles. Further, the long-term stability was investigated for 30 days in the absence and presence of 1 mM ACP and the obtained current responses are shown in Fig. 6B. At the end of 30 days, the developed sensor could retain >95% and >91% of its initial current response in the absence and presence of ACP, respectively. Furthermore, the reproducibility of the sensor fabrication methodology was investigated by fabricating five CHCF-FMF/GCE sensors separately using the same protocol and examined their current responses. Fig. 6C shows the obtained current response of five individually fabricated CHCF-FMF/GCE in the absence and presence of 1 mM ACP, which showed the relative standard deviation (%RSD) of <2.5% and <3.6%, respectively. It demonstrates the excellent electrode-to-electrode reproducibility of the designed sensor. The selectivity of CHCF-FMF/GCE was investigated by performing DPV with 1 mM of ACP and 0.5 mM of various interfering species such as uric acid, urea, sulfite, cholesterol, glucose, dopamine, ascorbic acid, sodium chloride, hydrogen peroxide, NADH, bisphenol-A, L-cysteine in 0.1 M KCl solution. The obtained current responses are shown in Fig. 6D, and it can be seen that the proposed sensor is highly selective for ACP, and it did not show any quantifiable signal for the interfering species except DA and AA, which were also <5%. These results exhibit that the proposed sensor is highly stable, reproducible, and selective towards ACP, which could be attributed to the effective integration of CHCF in the FMF framework. Further, this superior response inspired us to explore the applicability of the proposed sensor towards ACP determination in real-life samples.

3.5. Practical applicability of CHCF-FMF/GCE

The practical application of the fabricated sensor was studied by utilizing them for the detection of ACP in biofluids, pharmaceutical formulations and environmental samples. In the case of biofluids, human and rabbit serum samples were diluted with 0.1 M KCl solution, and the real sample analysis was performed. Following the standard addition method, known concentrations of ACPs were spiked into the diluted serum samples and the obtained DPVs are shown in Fig. S6 and S7. In the case of environmental sample, the facet water was diluted with 0.1 M KCl and taken in the electrochemical cell, to which known concentrations of ACP were added by following the standard addition method (Fig. S8). In the case of pharmaceutical formulations, known concentrations of tablet stock solutions were spiked in 0.1 M KCl electrolyte and the obtained DPVs are depicted in Fig. S9. The developed sensor demonstrated excellent electrocatalytic activities in diluted serum, environmental and pharmaceutical samples, with recoveries

ranging from 96.2% to 106.2%, as shown in Table 2.

4. Conclusions

In the present work, a facile and cost-effective electrochemical sensor was sustainably developed for the selective sensing of micromolar to millimolar concentrations of ACP in diverse environments using cobalt hexacyanoferrate decorated iron terephthalate MOF (CHCF-FMF). The sensor displayed excellent electrocatalytic activity towards ACP, along with remarkable stability, good reproducibility, acceptable repeatability, and no cross-reactivity against common interferents. The superior performance of the fabricated system could be attributed to the effective integration of FMF and CHCF as a result of *in-situ* formation, which synergistically improved the overall performance of the designed sensor towards ACP determination. Further, the sensor was extended for ACP sensing in practical samples such as human and rabbit serum samples, commercial tablets, and facet water, which showed acceptable recoveries. Therefore, the developed sensor could be potentially employed for medical diagnostic, point-of-care, drug, and environmental monitoring. Besides, efforts are underway to construct a flexible and disposable substrate for the proposed sensor, aiming to pave the way for the development of handheld portable ACP sensor devices. These devices hold potential for transformative applications in healthcare, industry, and environmental monitoring.

CRedit authorship contribution statement

K Theyagarajan: Writing – review & editing, Writing – original draft, Visualization, Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation. **Buddolla Anantha Lakshmi:** Software, Investigation, Formal analysis, Data curation. **Young-Joon Kim:** Validation, Supervision, Resources, Funding acquisition, Conceptualization, Writing – review & editing.

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.2024.144229](https://doi.org/10.1016/j.electacta.2024.144229).

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