

Water-induced supramolecular self-assembly of porphyrin integrated with multivalent metal–organic framework for enhanced electrochemiluminescence and ultrasensitive aptasensing of 4-fluoromethamphetamine

Bingxue Fan

Changzhou University

Ding Jiang

Changzhou University

Yuan Ni

Changzhou University

Tengfei Meng

Changzhou University

Zheng Sun

Changzhou Municipal Security Bureau

Haibo Li

Changzhou Municipal Security Bureau

Wenchang Wang

Changzhou University

Zhidong Chen

zdchen@cczu.edu.cn

Changzhou University

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Abstract

Aggregation-caused quenching (ACQ) and poor aqueous solubility severely restrict electrochemiluminescence (ECL) applications of polycyclic aromatic hydrocarbons (PAHs). Herein, a water-induced supramolecular self-assembly strategy is proposed to address these drawbacks. Via a simple reprecipitation route, representative PAH meso-tetrakis(4-carboxyphenyl)porphyrin (TCPP) forms ordered supramolecular aggregates driven by noncovalent interactions, which suppress π - π stacking and ACQ and achieve a low triggering potential of -1.0 V. Iron-based MOF supported molybdenum disulfide (MIL-101@MoS₂) is adopted as a multifunctional amplifier: reversible valence interconversion of Fe²⁺/Fe³⁺ and Mo⁴⁺/Mo⁶⁺ sustains continuous redox cycling to improve redox activity, while abundant oxygen vacancies accelerate electron transfer and coreactant activation for further ECL enhancement. After preparing MIL-101(Fe)@MoS₂@TCPP nanoparticles (MMST), an ECL aptasensor is fabricated for 4-fluoromethamphetamine (4-FMA) determination relying on target-triggered cyanine dye displacement. This sensor exhibits an ultralow limit of detection of (1.87×10^{-15} g/L) (S/N = 3) and a broad linear range from (1.0×10^{-14} – 1.0×10^{-6} g/L) g/L. It also shows favorable analytical results for real e-cigarette samples, with recoveries of 95.0–104.0% and relative standard deviations (RSD) less than 5.0%. This work offers a green route for high-performance PAH-based ECL luminophores and a reliable tool for rapid field screening of emerging psychoactive contaminants in complicated food-related matrices.

INTRODUCTION

New psychoactive substances (NPS) are synthetic drug analogs artificially fabricated by modifying the chemical structures of controlled substances to evade legal supervision, and they can induce equivalent or even stronger stimulant, hallucinogenic, and anesthetic effects than traditional illicit drugs.[1, 2] As the third-generation emerging drugs following traditional and synthetic drugs, NPS have posed severe challenges to global public security governance and forensic toxicology detection systems. 4-Fluoromethamphetamine (4-FMA) is a typical amphetamine-type NPS, which exhibits stronger neurostimulatory and hallucinogenic activities and higher abuse risks compared with amphetamine and methamphetamine.[3, 4] Nevertheless, the toxicological characteristics and supporting precise detection systems of 4-FMA remain poorly established due to its late emergence and regulatory implementation. Currently, high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS) serves as the mainstream detection method for 4-FMA.[5] Despite its high sensitivity and accuracy, HPLC-MS/MS suffers from cumbersome sample pretreatment procedures, high detection costs, and heavy reliance on large-scale precision instruments, which severely restricts its scalable applications in grassroots drug control monitoring and on-site law enforcement, and fails to meet the core demand for rapid on-site screening. Therefore, the development of efficient, rapid, facile, and field-deployable detection technologies for 4-FMA is urgently required in forensic toxicology and public security research.

Electrochemiluminescence (ECL) integrates the dual advantages of electrochemistry and photochemistry and has emerged as a high-specificity and ultra-sensitive analytical technique.[6–8] Featuring low background signal, excellent sensitivity, and tunable reaction controllability,[9, 10] ECL has become a promising alternative technique for rapid 4-FMA detection and has been widely applied in biomarker analysis, food safety assessment, immunoassay, and water quality monitoring.[11–13] In recent years, the concept of aggregation-induced electrochemiluminescence (AIECL) has attracted extensive research attention and promoted the innovation of ECL sensing technology.[14, 15] AIECL provides a feasible strategy to address the inherent aggregation-caused quenching (ACQ) effect and poor water solubility of conventional organic luminophores, which have long been the core bottlenecks limiting the practical applications of high-performance ECL sensors.[16, 17] Polycyclic aromatic hydrocarbons (PAHs) are a class of high-performance ECL luminophores, and mitigating their ACQ effect is critical for the construction of advanced ECL sensing platforms. Our previous work successfully inhibited the ACQ effect and improved the luminescence stability of PAHs by immobilizing PAH molecules within metal–organic framework (MOF) matrices via coordination anchoring.[18] However, conventional MOF-based composite luminophores are predominantly fabricated via solvothermal methods, which involve long reaction durations, complicated synthetic procedures, expensive organic solvents, and harsh high-temperature and high-pressure conditions. These limitations hinder the low-cost and large-scale preparation of MOF composites and severely restrict their practical deployment in on-site detection.

A reprecipitation strategy addresses the intrinsic drawbacks of poor water solubility and severe aggregation-caused quenching of PAHs, [19, 20] and proposes a facile, green, and efficient route to alleviate the ACQ effect of meso-tetrakis(4-carboxyphenyl)porphyrin (TCPP), a representative PAH luminophore. Driven by noncovalent intermolecular interactions, TCPP molecules spontaneously self-assemble into highly ordered and structurally stable supramolecular architectures in aqueous media.[21, 22] Such well-defined supramolecular structures effectively optimize interfacial electron transfer and energy migration, fundamentally mitigating the ACQ behavior and substantially boosting ECL performance. However, the stability and signal amplification capability of these self-assembled nano-architectures alone still face challenges in meeting the demands of ultra-trace detection. In order to solve this problem, it is imperative to introduce strategies that can further stabilize the luminophore and amplify the ECL response.

Recent studies have demonstrated that various strategies—including antenna effect-coupled Schottky heterojunctions,[23] co-reactant enrichment,[24] core–shell structures,[25] and band gap modulation[26]—can effectively stabilize luminophores and amplify ECL responses. In contrast to these approaches, MOF materials exhibit unique carrier advantages by virtue of their three-dimensional porous structures and the synergistic effect of multivalent metal centers.[27, 28] They can effectively disperse luminescent molecules, inhibit aggregation-induced deactivation, and remarkably improve the intensity and stability of ECL signals.[29, 30] More importantly, MOFs containing multivalent metal elements can continuously drive the redox cycling reactions in ECL systems through reversible valence-state conversion of metal nodes and ligands.[31–34] This multivalent cycling can significantly accelerate coreactant activation

while also lowering the ECL trigger voltage to -1.0 V by facilitating electron transfer and reducing kinetic barriers. Such valence-variable behaviors not only enhance the redox activity of luminophores but also precisely regulate the ECL reaction kinetics, thereby achieving further amplification and stabilization of sensing signals.[35, 36]

In this work, iron-based MOF supported molybdenum disulfide (MIL-101@MoS₂) was adopted as a multifunctional signal amplification carrier. Combined with the water-induced supramolecular self-assembly of TCPP, a novel ECL sensing platform with low trigger voltage, high stability and excellent sensitivity was successfully constructed. To achieve the ultra-sensitive and specific detection of 4-fluoromethamphetamine (4-FMA) in complex matrices, a label-free DNA-cyanine dye (DNA-Cy7) ECL aptasensor was further fabricated based on the specific recognition capability of nucleic acid aptamers. [37–39] In this sensing system, the target 4-FMA competitively displaces Cy7 dye molecules from the aptamer strand, thereby generating a specific ECL response. This detection procedure eliminates complicated separation and labeling operations, which greatly simplifies the analytical process. This finding fills the technical gap in the low-voltage and low-energy-consumption detection of 4-FMA and provides a desirable luminescent medium for the development of portable ECL detection devices. The constructed anti-interference and label-free sensing system enables reliable detection of 4-FMA in e-liquid samples and can be further extended to the rapid screening of adulterants in complex food matrices, including functional beverages, condiments and dietary supplements. The green and facile porphyrin supramolecular assembly strategy proposed in this study effectively addresses the inherent ACQ defect of conventional porphyrin luminophores, realizing the ultra-sensitive and convenient detection of 4-FMA in complex real samples. Compared with traditional large-scale mass spectrometry, this method exhibits prominent advantages of high efficiency, portability and low cost, holding great application potential in drug control, public security monitoring, forensic toxicology analysis and food safety detection. This work establishes a green and facile porphyrin supramolecular assembly strategy for high-performance ECL emitters and provides a universal analytical methodology for rapid screening of emerging contaminants in complex matrices.

EXPERIMENTAL SECTION

Reagents and materials, as well as the apparatus and characterization. The reagents and materials, as well as the apparatus and characterization, were described in the Supporting Information.

Preparation of TCPP NPs. TCPP NPs were prepared through a simple precipitation method using tetrahydrofuran (THF) and water as good and poor solvents. First, 0.001 g of TCPP was dispersed in 10 mL THF and dissolved under vigorous stirring; then, the mixture was poured into 20 mL of water rapidly under high-power sonication. Subsequently, continuous ultrasound experiment was carried out on the mixture until the solution became homogeneous. Finally, the mixture was transferred into a vacuum freeze dryer for 48 h and TCPP NPs were collected.

Preparation of MIL-101(Fe)@MoS₂@TCPP NPs (MMST). The detailed preparation of MIL-101(Fe)@MoS₂ was provided in the Supplement Information. Different from the preparation of nanoparticles above, the MMST was prepared by changing the water into MMS aqueous solution with different concentrations. In short, a certain amount of MMS was added into 20 mL of ultrapure water and sonicated for 30 min. Subsequently, 1 mg/mL of TCPP solution was quickly poured into 20 mL of MMS aqueous solution. Finally, the MMST was collected by vacuum freeze-drying.

ECL Measurement. Scheme 1 illustrates the preparation process for ECL sensors. After careful polishing with 0.3 and 0.05 μm of alumina powder on fine grinding paper, the glassy carbon electrode (GCE, $\phi = 3$ mm) undergoes ultrasonic cleaning with water and ethanol prior to use. Then, MMST (4 μL , 0.5 mg/mL) were dripped onto the electrode surface and dried naturally in turn. Then, Cy7-aptamer (4 μL , 3 μM) was dripped on the electrode surface and incubated overnight at 4°C. The constructed biosensor was tested in 50 mM K₂S₂O₈/phosphate buffered saline (PBS) (pH = 7.4) through ECL with -1.0 to 0 V and the scanning rate of 100 mV/s. The photomultiplier tube (PMT) was 800 V.

Scheme 1. Schematic illustration of the ECL aptasensor construction for 4-FMA detection.

RESULTS AND DISCUSSION

Characterisation of materials. The morphologies of the as-prepared materials were characterized using scanning electron microscopy (SEM) and field-emission scanning electron microscopy (FE-SEM). Self-assembled TCPP nanoparticles (TCPP NPs) were prepared via a straightforward rapid solution dispersion method as reported in a previous study.[20] To investigate the structural properties of water-induced porphyrin nanoparticles, a series of characterizations were conducted. The morphology of TCPP NPs was obtained by SEM, as shown in Fig. 1B. The water-induced effect transformed the originally irregular bulk structure (Figure S1) of porphyrin into a nanosheet-like morphology with lengths ranging from approximately 1 μm to 50 μm . As illustrated in Fig. 1A, MMS was synthesized using a facile hydrothermal method. The FE-SEM image of MMS (Fig. 1C) reveals a flower-like structure composed of an array of rough nanosheets. This unique flower-like ring structure consists of MIL-101(Fe) and MoS₂ arrays. Furthermore, the morphology of the MMST composite is displayed in Fig. 1D, where MMS and TCPP supramolecules are closely interconnected. The small-sized MMS particles are uniformly anchored onto the sheet-like structure of the TCPP supramolecules, accompanied by an increase in the diameter of TCPP NPs, which is attributed to the high dispersibility of MMS.

To identify the functional groups and chemical bonds of the as-prepared samples, Fourier transform infrared (FT-IR) spectroscopy was conducted. The water-induced porphyrin supramolecules generally exhibit an FT-IR spectrum consistent with that of TCPP, as shown in Fig. 2A. FT-IR analysis of TCPP NPs, MMS, and MMST (Figure S2) revealed distinct structural changes: the appearance of Mo-O and C-O-C stretching vibrations in MMST, accompanied by a reduction in surface hydroxyl (-OH) groups, verified the successful chemical coupling between MMS and TCPP NPs. The UV-Vis absorption spectra show (Figure S3) that MMST retains both the characteristic absorption of MMS in the UV region and the typical

Soret band of TCPP NPs at ~ 420 nm, confirming the successful integration of TCPP into the composite. Furthermore, to explore the crystal structure of the obtained materials, X-ray diffraction (XRD) analysis was performed. XRD analysis of TCPP and TCPP NPs (Figure S4) revealed that pure TCPP has well-defined crystalline peaks, whereas TCPP NPs exhibit broad and weak diffraction signals, confirming that the self-assembly process leads to the destruction of long-range order and the formation of low-crystallinity nanoparticles. As illustrated in Fig. 2B, the XRD intensity of TCPP NPs is significantly lower than that of porphyrin, which is likely attributable to the nanosizing process. In the case of MMST, the characteristic peaks include both the typical diffraction peaks of MoS_2 and those of MIL-101(Fe). Specifically, four weak diffraction peaks at $2\theta = 14.4^\circ$, 32.7° , 39.5° , and 58.3° correspond to the (002), (100), (103), and (110) crystal planes of MoS_2 (PDF#37-1492), respectively. Additionally, the diffraction peaks of MIL-101(Fe) (CCDC No. 605510) are also present.

Finally, the chemical composition and elemental valence states of MMST were analyzed using X-ray photoelectron spectroscopy (XPS) and energy-dispersive X-ray spectroscopy (EDS). Figure 2C reveals the presence of five elements—C, O, S, Mo, and Fe—in MMST. EDS analysis (Figure S5) further demonstrates the uniform presence and favorable distribution of these elements, consistent with the XPS results shown in Fig. 2C, thereby confirming the successful fabrication of the MMST composite. To further investigate the chemical states of the catalyst, the Fe 2p, S 2p, and Mo 3d spectra were examined. Figure 2D displays the high-resolution Fe 2p spectrum, where peaks at 710.57 and 724.17 eV correspond to Fe^{2+} in the $2p_{3/2}$ and $2p_{1/2}$ orbitals, respectively, while peaks at 712.96 and 726.85 eV are attributed to Fe^{3+} in the $2p_{3/2}$ and $2p_{1/2}$ orbitals, indicating the coexistence of $\text{Fe}^{2+}/\text{Fe}^{3+}$ in MMST.[40] Additionally, satellite peaks are located at 720.05 and 733.01 eV. In the S 2p spectrum (Fig. 2E), the binding energies of S $2p_{3/2}$ (161.59 eV) and S $2p_{1/2}$ (162.70 eV) are assigned to the S^{2-} orbital,[41] suggesting the presence of sulfur species and Fe–S bonds on the MMST surface. The peaks at 168.83 and 163.36 eV correspond to sulfate species ($-\text{SO}_4^{2-}$) and unsaturated edge S, respectively.[42] The high-resolution Mo 3d spectrum of MMST is deconvoluted into four peaks at 226.06, 229.00, 232.47, and 236.00 eV. The predominant peaks at 229.00 and 232.47 eV are assigned to Mo $3d_{5/2}$ and Mo $3d_{3/2}$, respectively, indicating the presence of Mo^{4+} (Fig. 2F). The small peak at 225.71 eV, arising from Mo–S bonding, is attributed to S 2s. Another peak at 336 eV is ascribed to Mo^{6+} oxide species formed during the in situ synthesis of MMST.[43] The high-resolution XPS spectra of O 1s and C 1s are shown in Figure S6 and Figure S7. Based on the above results, multiple active sites, including $\text{Fe}^{3+}/\text{Fe}^{2+}$, $\text{Mo}^{6+}/\text{Mo}^{4+}$, and various sulfur species, coexist in MMST.

The ECL enhancement mechanism of MMST. To investigate the origin of the enhanced ECL performance of TCPP NPs, Raman spectroscopy was first employed. By focusing on the characteristic peaks at 1366 cm^{-1} (designated as peak I) and 1560 cm^{-1} (designated as peak II), which are sensitive to structural changes in the porphyrin ring, the ratio of the relative intensities of these two vibrational peaks was calculated to evaluate the degree of π – π stacking.[7] The results show that TCPP NPs exhibit a relative peak intensity ratio of 0.59, which is approximately 0.09 lower than that of TCPP (0.67), indicating a relatively weaker π – π stacking in TCPP NPs. This finding reasonably explains that although

porphyrin, as a planar polycyclic aromatic hydrocarbon, tends to form aggregated states via intermolecular π - π stacking, the reduced π - π stacking in TCPP NPs may attenuate the ACQ effect, thereby enhancing the luminescence efficiency of the luminophores.[44]

To further explore the influence of π - π stacking on the optical properties, ultraviolet-visible (UV-Vis) absorption spectroscopy was conducted. Compared with the corresponding spectrum of the porphyrin solution, the UV-Vis spectrum of the porphyrin nanoparticles exhibits pronounced differences. The absorption spectrum of TCPP displays a classical Soret band and four Q bands, which are characteristic features of porphyrin. In comparison with TCPP, TCPP NPs show a blue shift of these bands and a decrease in absorbance, which are hallmark signatures of J-type (edge-to-edge) aggregation of TCPP molecules, likely induced by supramolecular interactions. This effectively restricts the aggregation of porphyrin molecules. Furthermore, the band gaps of TCPP and TCPP NPs were derived from Tauc plots. TCPP NPs exhibit a narrower band gap than TCPP, which is favorable for ECL emission. Collectively, these analyses clearly demonstrate that the optical properties of porphyrin can be effectively modulated by tuning its molecular structure. The water-induced effect not only alters the morphological structure of porphyrin but also influences its π - π stacking degree and optical characteristics, thereby opening new possibilities for the application of porphyrin in fields such as ECL.

Moreover, the high-resolution O 1s XPS spectrum shows a dominant peak at 531.57 eV assigned to defective Mo-O species, implying the formation of oxygen vacancies in the MMST composite. Combined with the EPR signal at $g \approx 2.000$ originating from unpaired electrons trapped in oxygen vacancies, XPS and EPR (Figure S8) mutually confirm the rich oxygen vacancy defects of MMST. These oxygen vacancies serve as active centers to accelerate charge transfer and promote the activation of $S_2O_8^{2-}$ coreactant, thereby greatly improving the ECL emission efficiency.

To further verify the suppression of the ACQ effect in TCPP NPs, time-resolved fluorescence decay measurements were carried out. As depicted in Fig. 3D and 3E, TCPP NPs exhibit a distinctly prolonged fluorescence lifetime ($\tau = 11.60$ ns) in comparison with monomeric TCPP ($\tau = 10.60$ ns). Typically, the severe π - π stacking formed in aggregated polycyclic aromatic hydrocarbon (PAH) aggregates dominates the ACQ effect, which accelerates non-radiative decay and thus shortens the excited-state lifetime of luminophores. The obvious extension in the fluorescence lifetime of self-assembled TCPP NPs demonstrates that water-induced supramolecular assembly effectively restricts the unfavorable intermolecular π - π stacking and inhibits non-radiative energy dissipation. Benefiting from the prolonged excited-state lifetime, a higher population of excited-state TCPP luminophores can be well maintained, which is favorable for efficient luminescence and ECL emission.

To verify that the cyanine dye can be displaced from the DNA-cyanine dye aptamer in the presence of 4-FMA, UV-Vis absorption spectroscopy was performed on APT/Cy7 and 4-FMA/APT/Cy7 solutions, with particular attention to the absorption peaks at 670 nm and 780 nm. As shown in Fig. 3F, the absorption spectra of the two solutions nearly completely overlap around 550 nm and 880 nm, indicating that the total dye concentration and optical path conditions are consistent between samples, thereby ruling out

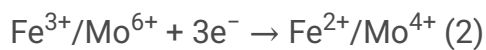
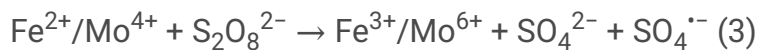
dilution or injection errors. In contrast, within the range of 660–780 nm, the absorbance of APT/Cy7 is markedly higher than that of 4-FMA/APT/Cy7. This selective decrease in absorbance upon addition of 4-FMA suggests a reduced contribution of the cyanine dye in the characteristic absorption region of the bound state, consistent with the spectral signature of dye displacement from the aptamer by 4-FMA. Therefore, this method enables label-free detection by directly monitoring the 4-FMA-induced displacement reaction via UV-Vis spectroscopy, without the need for laborious separation steps.

In this work, $K_2S_2O_8$ was employed as the coreactant, TCPN NPs served as the luminophore, and the MOF-based material MMS acted as the luminophore carrier, which effectively enhanced the ECL performance of the luminophore. The as-prepared composite MMST was subsequently utilized as the final cathodic ECL emitter in the sensing system. The proposed ECL mechanism of the MMST/ $K_2S_2O_8$ system can be expressed as follows: In route 1, a small number of $S_2O_8^{2-}$ gained electrons to produce $SO_4^{\cdot-}$ (Eq. (1)), which reacted with MMST to produce a moderate ECL signal. In route 2, Fe^{3+} and Mo^{6+} captured electrons for conversion to lower valence states (Fe^{2+} and Mo^{4+}) (Eq. (2)), which accelerated the catalytic decomposition of $S_2O_8^{2-}$ and consistently produced a large amount of $SO_4^{\cdot-}$ (Eq. (3)), enhancing the ECL signals and realizing a reversible transition of the valence state of the metal ions. In route 3, the rich oxygen vacancies in the composite could adsorb and activate dissolved O_2 , which was reduced to H_2O_2 (Eq. (4)), and $OH^{\cdot}$ was formed by reacting variable valence metal ions with H_2O_2 (Eq. (5)), which further reacted with $S_2O_8^{2-}$ to generate more $SO_4^{\cdot-}$ (Eq. (6)), achieving superimposed amplification of ECL signals. In the ECL emission route, the ground state MMST first gained electrons to become $MMST^{\cdot-}$ (Eq. (7)), which subsequently reacted with $SO_4^{\cdot-}$ to produce the excited state ($MMST^*$) (Eq. (8)). Finally, $MMST^*$ produced ECL emission and returned to MMST (Eq. (9)), and the corresponding mechanism equations were as follows:

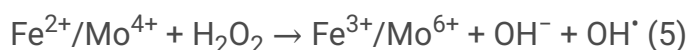
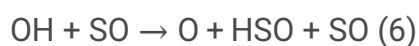
Route 1:



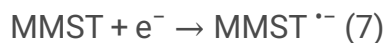
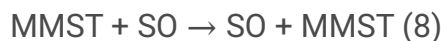
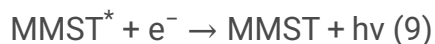
Route 2:



Route 3:



ECL emission:



Electrochemical Characterization of the Modified Electrode. The stepwise construction of the sensor was characterized by electrochemical impedance spectroscopy (EIS). As shown in Fig. 4A, the bare glassy carbon electrode (GCE) exhibits the smallest impedance (curve a). After modification with MMST, a significant increase in impedance is observed (curve b), which is attributed to the poor conductivity of MMS, thereby hindering electron transfer at the electrode surface. Upon further modification of the MMST/GCE with the aptamer, the impedance increases further (curve c) due to steric hindrance effects. Subsequently, after incubating the resulting DNA-Cy7/MMST/GCE with a solution containing the target analyte 4-FMA, the specific binding between DNA-Cy7 and the analyte occurs, leading to the displacement of Cy7. Consequently, no substantial change in impedance is observed (curve d). These results collectively confirm the successful fabrication of the ECL aptasensor.

In parallel, cyclic voltammetry (CV) was employed to monitor the interfacial current variations during each modification step of the sensor fabrication process. As depicted in Fig. 4B, upon modification of GCE with MMST, the redox current of the composite decreases markedly (curve b), which is consistent with the diminished electron transport capability of MMST. Following the immobilization of the aptamer DNA-Cy7 onto the electrode surface, the increased surface resistance leads to a reduced electron transfer rate, thereby further decreasing the current signal (curve c). Subsequently, after incubation with the target analyte 4-FMA, the peak current remains almost unchanged (curve d), which is attributable to the dye displacement effect. The EIS and CV results exhibit consistent trends in electron transfer behavior, collectively validating the successful assembly of the sensor.

To evaluate the feasibility of the proposed sensor, the electrochemiluminescence (ECL) behaviors of different modified electrodes were examined. As shown in Fig. 4C, with $\text{K}_2\text{S}_2\text{O}_8$ serving as the coreactant in the ECL reaction system, a weak ECL signal is observed at the bare GCE (curve a). Upon modification with the luminophore TCPP, the ECL signal increases slightly to approximately 1200 a.u. (curve b). In contrast, when TCPP NPs are modified onto the GCE, the ECL signal of the sensor exhibits an approximately six-fold enhancement compared to that of monomeric TCPP (curve c). This signal amplification is attributed to the water-induced porphyrin supramolecules effectively alleviating the aggregation-caused quenching (ACQ) effect, thereby generating stronger ECL emission. Furthermore, the ECL intensity of MMS alone is approximately 3000 a.u. (curve d), whereas the MMST composite achieves an ECL intensity close to 18000 a.u. (curve e). This enhancement arises from the presence of multivalent Fe and Mo ions in the MOF-based carrier MMS, whose valence state changes can actively participate in the ECL redox process, thereby boosting the ECL performance. Subsequently, upon further incubation of the aptamer DNA-Cy7 on the electrode, the ECL signal decreases (curve f) due to the steric

hindrance effect of the biomacromolecules, which impedes electron transfer. Finally, when the fabricated aptasensor is used for detection, the specific recognition and immobilization of the target analyte on the electrode surface lead to a further reduction in the ECL signal (curve g). These results collectively confirm the successful construction of the aptasensor.

Sensing Performance. To evaluate the sensitivity of the proposed ECL aptasensor, the ECL intensities in response to varying concentrations of 4-FMA were measured under optimal experimental conditions (Figure S9). As shown in Fig. 5A, the ECL intensity gradually increases with the concentration of 4-FMA ranging from 1.0×10^{-14} g/L to 1.0×10^{-6} g/L. A good linear relationship is observed between the enhanced ECL intensity (ΔI_{ECL}) and the logarithm of the 4-FMA concentration. The corresponding calibration curve is presented in Fig. 5B, yielding a linear regression equation of $\Delta I_{\text{ECL}} = 15433.83 + 856.41 \lg C_{4\text{-FMA}}$, with a correlation coefficient (R^2) of 0.985. The detection limit is determined to be 1.87×10^{-15} g/L ($S/N = 3$). These results demonstrate that the constructed aptasensing platform exhibits satisfactory sensitivity. Moreover, in comparison with many previously reported detection methods, the proposed ECL biosensor offers a lower detection limit and a wider linear range (Table S1).

The specificity, ECL signal stability, and reproducibility of the sensor are also of critical importance. Specificity serves as a key parameter for evaluating the detection capability of the designed sensor. The selectivity of the aptasensor was assessed using furanyl fentanyl, flu alprazolam, AB-PINACA, MDPV, RCS-4, and 4-CEC as interfering substances (chemical structures are shown in Figure S10). Briefly, the experimental procedure was identical to that used for 4-FMA detection, with the concentration of these interfering substances (1.0×10^{-4} g/L) being 10,000-fold higher than that of 4-FMA. As shown in Fig. 6A, the enhancement of the ECL signal induced by 4-FMA is markedly higher than that of the other NPS, indicating the favorable selectivity of the proposed sensor toward 4-FMA.

As illustrated in Fig. 6B, ten consecutive cyclic voltammetry scans were performed on different modified electrodes in the detection solution. The results demonstrate that each modified electrode exhibits excellent ECL signal stability, with relative standard deviation (RSD) values all below 5.0%. This finding strongly confirms the superior stability of the constructed sensor in terms of ECL signal output, thereby providing a reliable foundation for its practical application. Storage stability testing was conducted by placing the ECL aptasensor-modified glassy carbon electrode in a 4°C refrigerated environment. The experimental data (Fig. 6C) reveal that the ECL signal intensity of the sensor exhibits only a slight decreasing trend over storage durations of 0, 3, 9, 12, and 15 days. This result indicates the excellent storage stability of the constructed sensing platform, further validating the reliable stability of the ECL aptasensor system.

Under identical experimental conditions, five batches of independently prepared aptasensors were used to detect the same concentration of 4-FMA. The corresponding ECL response values were measured and recorded. The experimental data show that the RSD of the ECL intensities across the five sensor batches is below 5.0% (Fig. 6D), fully demonstrating the excellent detection reproducibility of the developed aptasensor system.

Detection of 4-FMA in real samples. To validate the feasibility of the proposed ECL method, a standard addition method was employed in this study. The specific procedure was as follows: known concentrations of 4-FMA standard solutions were added in a gradient manner to diluted e-cigarette samples, followed by quantitative analysis using the as-prepared ECL aptasensor. The spike recovery and relative standard deviation (RSD) were calculated based on the ratio of the measured concentration to the spiked concentration. As shown in the Table 1, the recoveries of the sensor range from 95.0% to 104.0%, with RSD values below 5%. These results strongly demonstrate that the proposed ECL aptasensor exhibits high applicability and favorable sensitivity for the detection of 4-FMA in e-cigarette samples.

Table 1
Analytical data of 4-FMA in the e-cigarettes samples with the as-developed approach (n = 3).

e-cigarettes 1	0	ND	-	-
Samples	Added	The ECL sensor		
Found (×10 ⁻⁸ g/L)	(×10 ⁻⁸ g/L)	Recovery(%)	RSD(%)	
1	0.95	95.0	3.3	
10	10.2	102	2.8	
100	97.2	97.2	2.9	
e-cigarettes 2	0	ND	-	-
	1	0.98	98	2.7
	10	10.4	104	3.9
	100	103.1	103.1	3.8
e-cigarettes 3	0	ND	-	-
	1	0.98	98	2.2
	10	10.4	104	3.9
	100	99.2	99.2	2.1

CONCLUSION

In this study, a simple reprecipitation method was employed to alleviate the ACQ effect of porphyrin molecules, yielding water-induced supramolecular assemblies with prolonged excited-state lifetimes and enhanced luminescence efficiency. Meanwhile, a multivalent metal–organic framework was utilized as the luminophore carrier, which not only effectively immobilized the luminophore but also actively participated in the ECL redox reactions through reversible valence state transitions of the multivalent ions. Specifically, the rapid cyclic interconversion of the Fe²⁺/Fe³⁺ and Mo⁴⁺/Mo⁶⁺ redox pairs

substantially enhanced the ECL response and lowered the trigger voltage to -1.0 V. The resulting MMST composite was successfully integrated into an ECL sensing platform for the ultrasensitive detection of 4-FMA in complex e-liquid matrices, achieving an exceptionally low detection limit of 1.87×10^{-15} g/L and a wide linear range spanning ten orders of magnitude ($1.0 \times 10^{-14} - 1.0 \times 10^{-6}$ g/L). Upon introduction of the target analyte, it specifically bound to the DNA-Cy7 aptamer, leading to the displacement of the cyanine dye Cy7 and significantly improving the specificity of the sensor. The satisfactory recoveries (95.0–104.0%) and low relative standard deviations ($< 5\%$) obtained in viscous, multi-component e-liquid samples containing propylene glycol, glycerol, nicotine, and flavoring agents demonstrated the robust matrix tolerance and operational reliability of the proposed platform. These analytical attributes establish a versatile analytical strategy for the detection of emerging contaminants in complex matrices, providing a methodological foundation for rapid on-site screening applications.

Declarations

ASSOCIATED CONTENT

Supporting Information for this article is available online at * * *.

Other experimental details, materials, methods, instruments, other characterizations, and supplementary figures S1-S10 and Table S1.

AUTHOR INFORMATION

Corresponding Author

Zhidong Chen – *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China ;*orcid.org/0000-0002-9383-9563; *E-mail address: zdchen@cczu.edu.cn*

Authors

Bingxue Fan – *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China*

Ding Jiang – *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China;* orcid.org/0000-0001-6600-4459

Yuan Ni – *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China*

Tengfei Meng– *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China*

Zheng Sun – *Institute of Forensic Science, Changzhou Municipal Security Bureau, Changzhou 213164, China*

Haibo Li – *Institute of Forensic Science, Changzhou Municipal Security Bureau, Changzhou 213164, China*

Wenchang Wang – *Jiangsu Key Laboratory of Advanced Catalytic Materials and Technology, School of Petrochemical Engineering, Changzhou University, Changzhou, Jiangsu, 213164, P. R. China*

Author Contributions

The manuscript was written through the contributions of all the authors. All the authors have given approval to the final version of the manuscript.

Conflict of interest

The authors confirm no declarations of interest.

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Scheme 1

Scheme 1 is available in the Supplementary Files section.

Figures

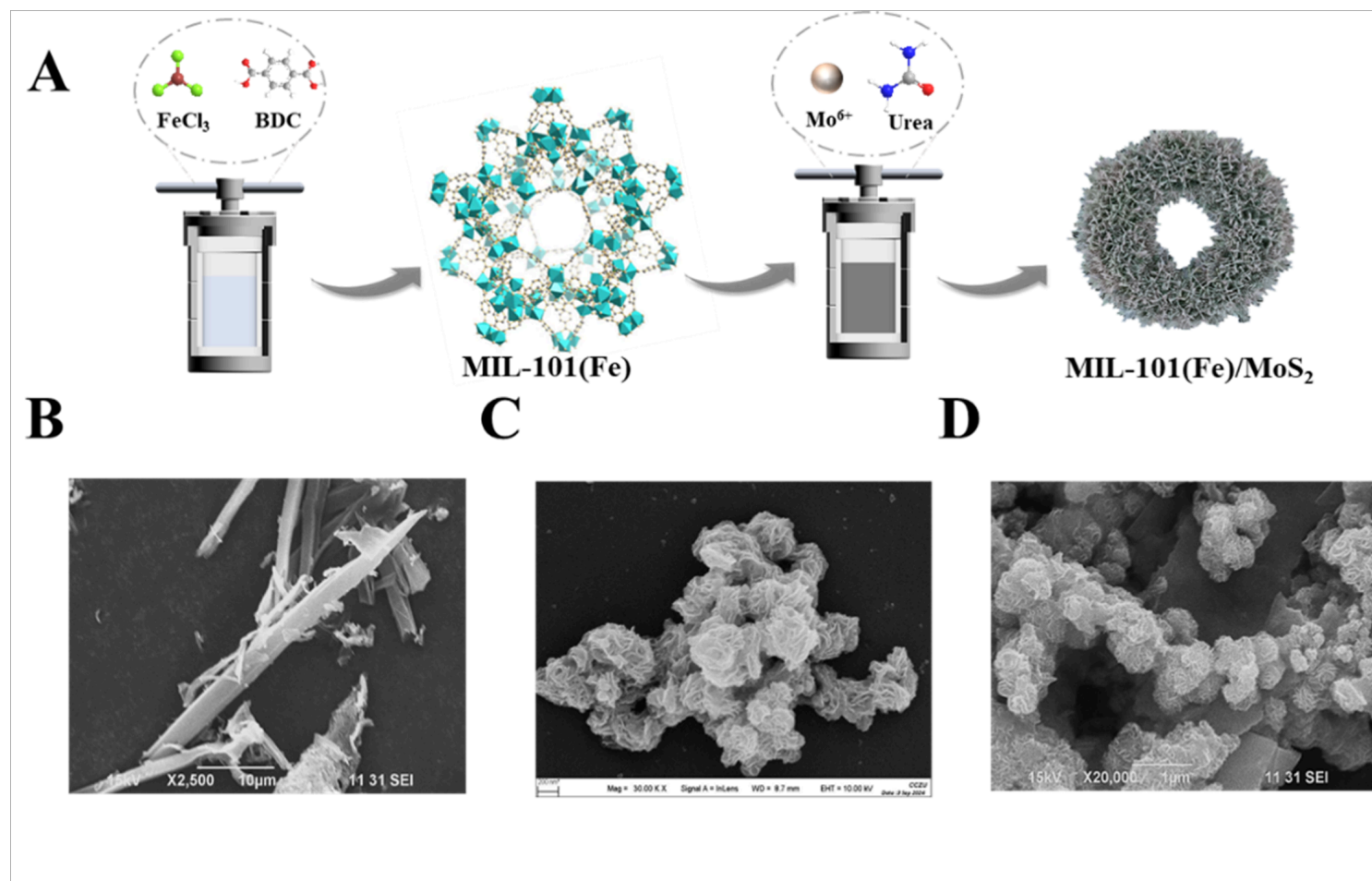


Figure 1

(A) Synthesis of MMS; (B) SEM image of TCPP NPs; (C) FE-SEM image of MMS; and (D) SEM image of MMST

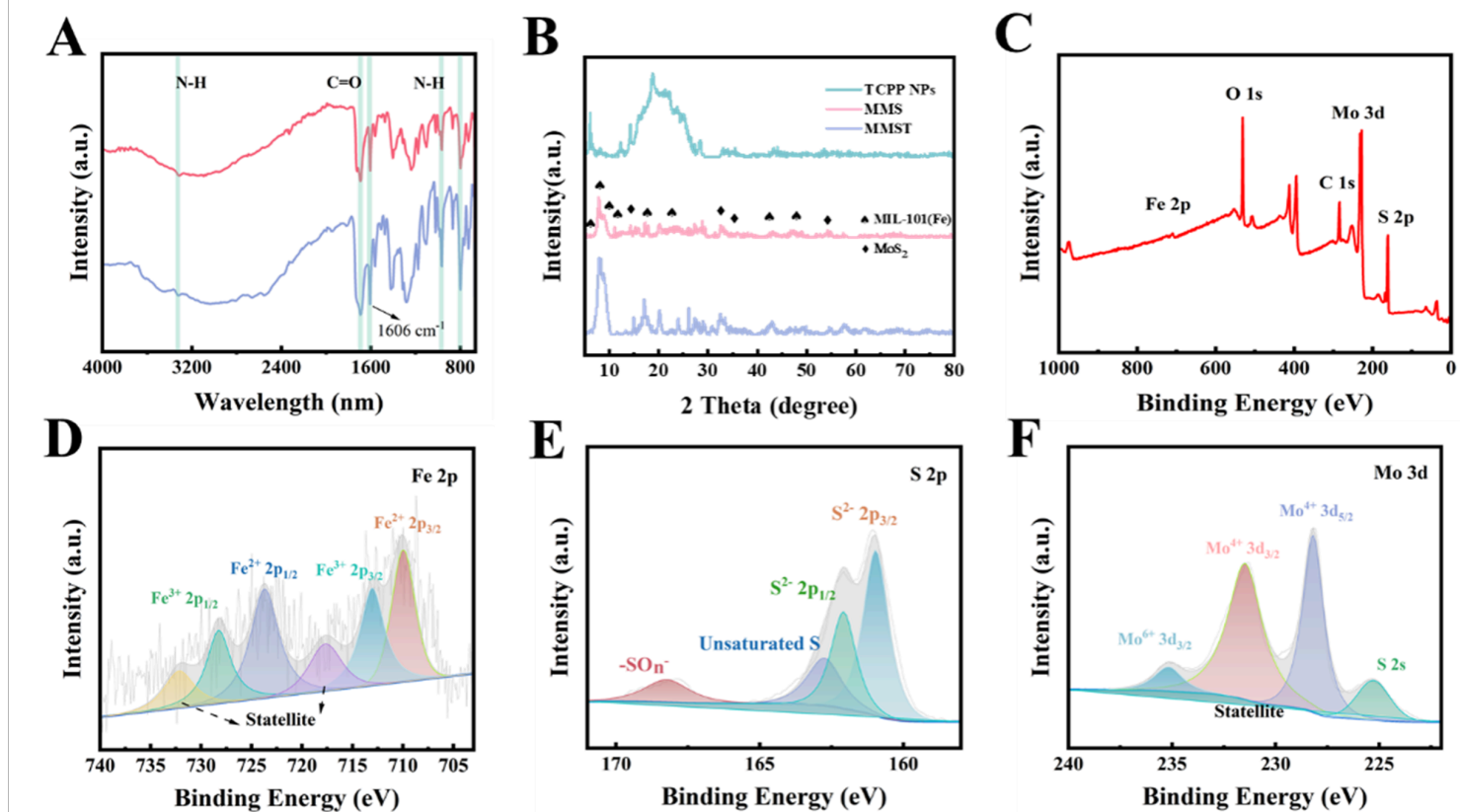


Figure 2

(A) FT-IR spectra of TCPP and TCPP NPs; (B) XRD patterns of different substances; (C) XPS spectrum of MMST; (D) high-resolution spectra of Fe 2p; (E) S 2p; (F) Mo 3d

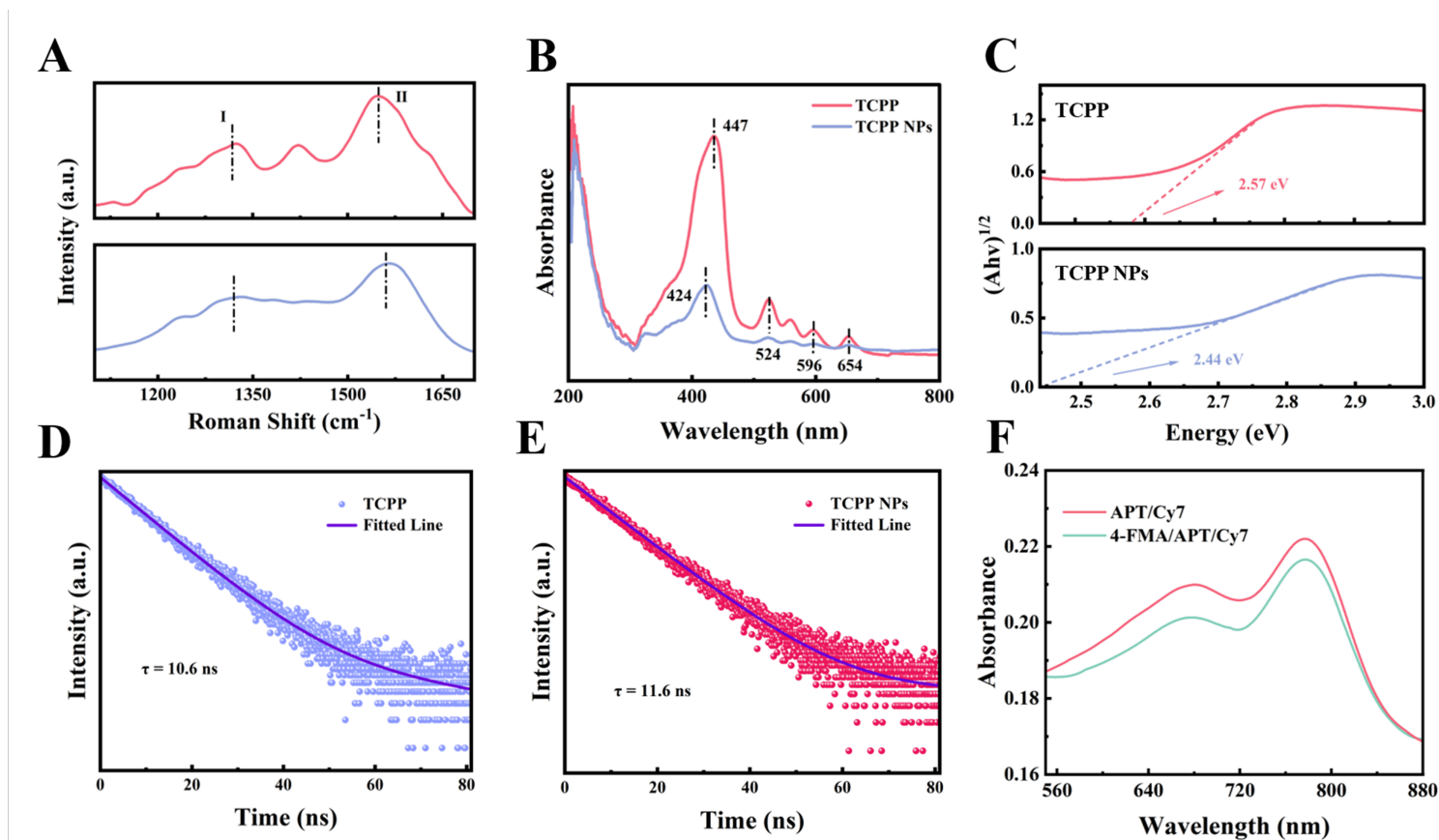


Figure 3

(A) Raman spectra (TCPP, red curve; TCPP NPs, blue curve), (B) UV–Vis absorption spectra, and (C) Tauc plots of TCPP and TCPP NPs; time-resolved fluorescence decay curves of (D) monomeric TCPP and (E) TCPP NPs ($\lambda_{\text{exc}} = 420 \text{ nm}$); and (F) UV–Vis absorption spectra of APT/Cy7 and 4-FMA/APT/Cy7.

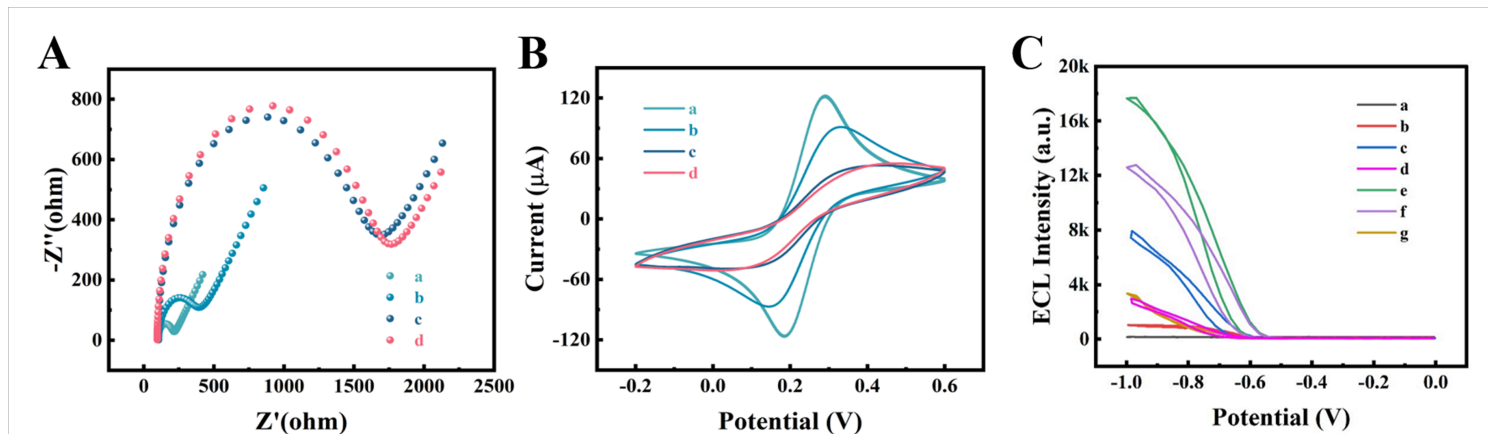


Figure 4

EIS (A) and CV curves (B) of different modified electrodes in 0.1 mol/L KCl and 10 mmol/L $\text{K}_3\text{Fe}(\text{CN})_6/\text{K}_4\text{Fe}(\text{CN})_6$ solution: GCE (a), MMST/GCE (b), DNA-Cy7/MMST/GCE(c) and 4-FMA/DNA-Cy7/MMST/GCE(d); the ECL-potential curves (C) of GCE (a), TCPP/GCE (b), TCPP NPs (c), MMS (d),

MMST/GCE (e), DNA-Cy7/MMST/GCE (f) and 4-FMA/DNA-Cy7/MMST/GCE (g) in 0.1 mol/L PBS (pH 7.4) containing 0.05 mol/L $K_2S_2O_8$ were obtained

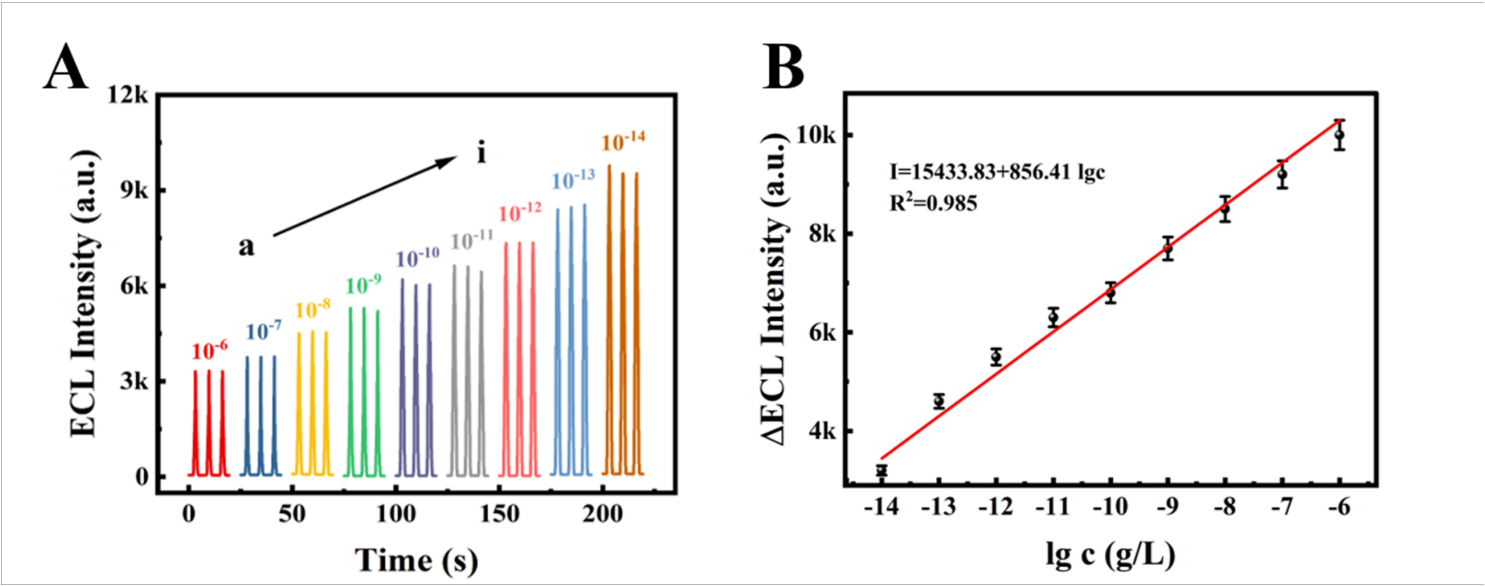


Figure 5

(A) The response range of ECL to different concentrations of 4-FMA is a–i: 1.0×10^{-6} g/L to 1.0×10^{-14} g/L; (B) Linear fit curve showing the relationship between 4-FMA concentration (1.0×10^{-6} g/L to 1.0×10^{-14} g/L) and Δ ECL

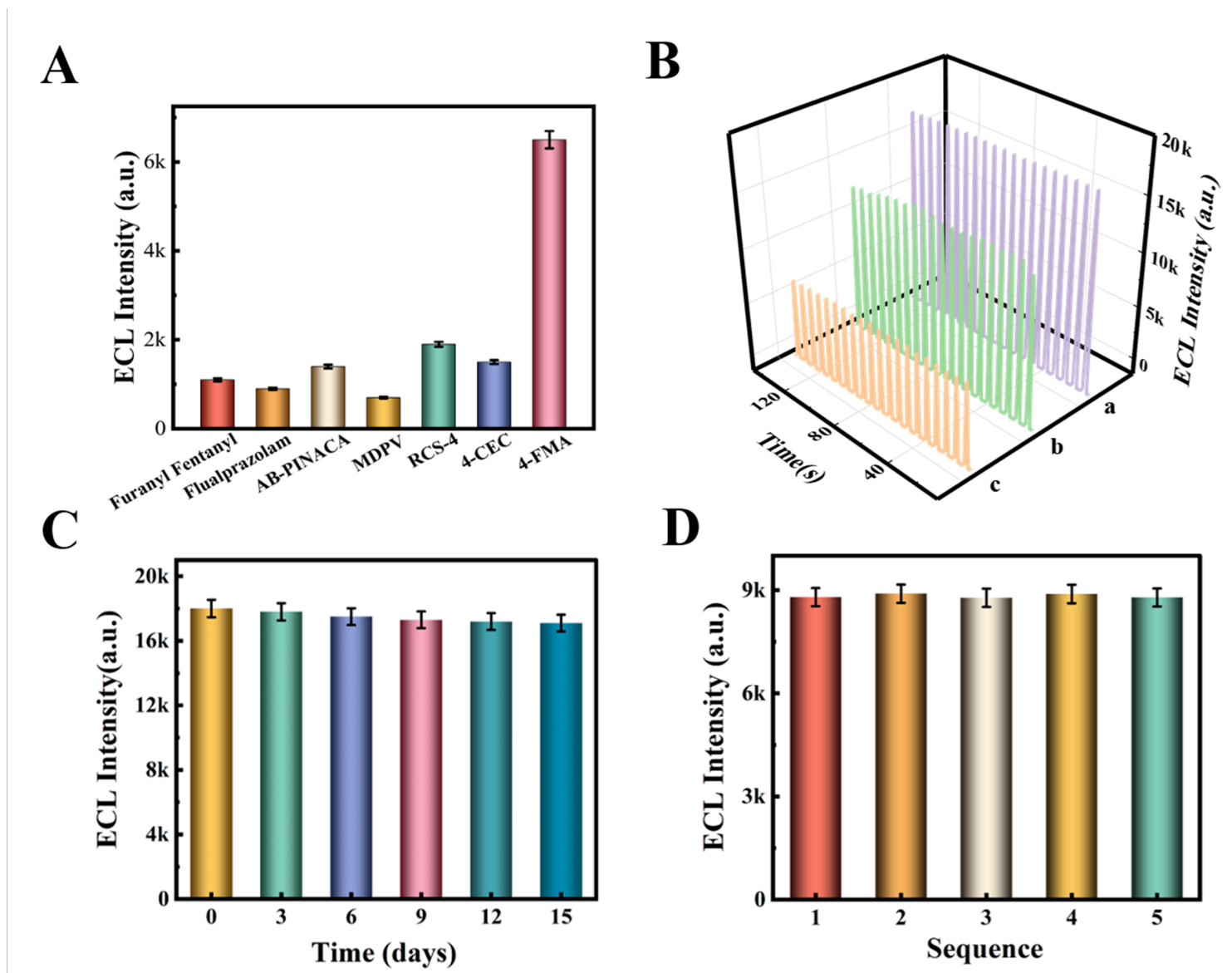


Figure 6

(A) Specificity of the aptasensor toward various interfering NPS; (B) ECL stability curves of MMST/GCE (a), DNA-Cy7/MMST/GCE (b), and 4-FMA/DNA-Cy7/MMST/GCE (c) over 10 consecutive scanning cycles in a buffer containing 0.05 mol/L $K_2S_2O_8$; (C) Long-term storage stability of the aptasensor; (D) Reproducibility of the aptasensor obtained from five parallel experiments.

Supplementary Files

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