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Silica Nanoparticles Modified Carbon Paste Electrode as a Voltammetric Sensor for Determination of Diclofenac

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The present study describes the use of a new carbon paste electrode modified by means of Silica nanoparticles prepared by a simple and rapid procedure for the determination of sodium diclofenac (DCF). Moreover, the present study focuses on the characterization of electrochemical impedance spectroscopy (EIS) and scanning electron microscopy (SEM) of the prepared Silica NPs-CPE. In this work, the electrochemical behavior of sodium diclofenac at the surface of Silica nanoparticles modified carbon paste electrode (Silica NPs-CPE) was examined using current voltammetric methods (cyclic voltammetry (CV) and the differential pulse voltammetry (DPV). The catalytic oxidation peak currents show a linear dependence on the diclofenac. Linear analytical curves were acquired in the ranges of 0.1-500.0 µM and at the detection limit of 0.046 µM. Furthermore, the proposed modified electrode exhibited a high sensitivity, an excellent reproducibility, good selectivity, and a successfully easy construction process. The present study also examined the interferences of foreign substances. The method was used for the determination of sodium diclofenac present in real samples.

Keywords: Silica nanoparticles, Modified carbon paste electrode, Sodium diclofenac, Cyclic voltammetry, Differential pulse voltammetry

INTRODUCTION

Diclofenac, known as the 2-[(2,6-dichloro phenyl) amino] benzene acetic acid, is a non-steroidal anti-inflammatory drug used for the treatment of different illnesses such as rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, osteoarthritis, *etc*. [1,2]. It is one of the most generally used painkillers clinically used as the sodium salt [3]. Many analytical methods have been used for DCF determination, including potentiometry [4], high performance liquid chromatography [5], capillary zone electrophoresis [6], thin layer chromatography [7], spectrofluorometry [8], gas chromatography [9] and spectrophotometric techniques [10].

Most of the methods reported in the literature are costly and need complex preconcentration as well as derivatization. Unlike other methods, electrochemical methods are characterized by portability, simplicity, minimal cost, and reasonably short analysis time. However, there are problems for the direct electrochemical oxidation of DCF at the usual electrode; for example, the electrochemical oxidation of DCF is so slow that almost no current response is observed at the usual electrodes. These problems can be solved through modification of electrodes. Various electrochemical procedures have been applied for the determination of DCF [11-20].

The electrochemical methods using nanoparticles carbon paste modified electrodes have been widely recognized as simple, sensitive, and selective analytical methods for the determination of trace amounts of biologically important compounds [21-30].

However, no DCF sensor has been reported on the basis of a nano-Silica carbon paste electrode. Since the Silica nanoparticles have large surface area and chemical stability, tunable porosity and, high thermal, recently there is a considerable interest in using Silica nanoparticles as a modifier. For the first time, the present study reports the

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voltammetric behavior of Silica nanoparticles modified carbon paste electrode for determination of DCF.

EXPERIMENTAL

Apparatus

Electrochemical experiments were carried out on Autolab PGSTAT12N potentiostat/galvanostat controlled using the GPES 4.9 software (Eco Chemie, The Netherlands) with a Metrohm voltammetry cell in a three-electrode form. An Ag/AgCl saturated KCl electrode, a platinum wire, and a modified-unmodified electrode were used as the reference, auxiliary and, working electrodes, respectively. A Metrohm 780 pH/ion meter was also used for pH measurements.

Reagents

The sodium diclofenac (DCF) was purchased from Sigma-Aldrich, and the graphite powder was bought from Fluka. All other chemicals used in this research were of analytical grade from Merck. For each experiment, doubly-distilled water was used.

Preparation of Silica Nanoparticles

40 mL of ethanol and 10 ml of de-ionized water were mixed with 1.0 ml of concentrated ammonia aqueous solution. The mixed solution was then homogenized by ultrasonic for 30 min to form a uniform dispersion. Subsequently, 7 ml of tetraethoxysilane (TEOS) was added dropwise into the solution with strong stirring. After stirred at room temperature for 6 h, the solution was centrifuged. Then, Silica nanoparticles were washed with deionized water for 3 times and dried in an oven at 50 °C for 12 h [31].

Electrode preparation

35 mg of the graphite powder was hand mixed with 10 mg Silica nanoparticles, and 5 mg paraffin oil in a mortar and pestle to manufacture a homogeneous carbon paste. The modified carbon paste was then packed into an insulin syringe. A copper wire was inserted into the carbon paste, and in this way, an electrical contact was created. When necessary, a new surface was acquired by pushing an excess of paste out of the syringe, which was then polished with weighing paper. Also, unmodified CPE was prepared in the same way without adding Silica nanoparticles to the mixture. These were utilized for the purpose of comparison.

RESULTS AND DISCUSSION

Characterization of SilicaNPsCPE Surface

Figure 1 shows the impedance plots for (a) the bare CPE and (b) the SilicaNPsCPE surfaces in 5.0 mM $[Fe(CN)_6]^{3-/4-}$ (1:1) solution in 0.1 M KCl. The values of the charge transfer resistance (Rct) were calculated for the bare CPE and the SilicaNPsCPE as 5.3 and 0.83 kΩ, respectively. Therefore, it is clear that the SilicaNPsCPE, rather than the bare CPE can increase the electron transfer.

The morphologies of modified and bare electrode surfaces were characterized by SEM in Fig. 2. It can be seen that the surface of the CPE consists of isolated and irregular carbon flakes (Fig. 2A). Figure 2B shows the SEM of SilicaNPsCPE. As it can be seen, the spherical Silica nanoparticles were distributed uniformly on the surface of carbon paste.

The microscopic areas of the bare CPE and the Silica NPs-CPE were evaluated by cyclic voltammetry by 5 mM $K_3Fe(CN)_6$ solution in 0.1 M KCl as a probe at different scan rates [32]. For a reversible process, the Randles-Sevcik equation is used:

$$I_{pa} = 2.69 \times 10^5 n^{3/2} A C_o D_R^{1/2} v^{1/2} \quad (1)$$

where I_{pa} is the anodic peak current, A is the surface area of the electrode, n is the electron transfer number, D_R is the diffusion coefficient, C_O is the concentration of $K_3Fe(CN)_6$, and v is the scan rate. For 5 mM $K_3Fe(CN)_6$ in the 0.1 M KCl electrolyte, n = 1, $D_R = 7.6 \times 10^{-6}$ cm^2 s^{-1}, the surface area of electrodes can be calculated from the slope of the I_{pa}-$v^{1/2}$ relation. In CPE and Silica NPs-CPE, the electrode surfaces were 0.023 and 0.028 cm^2, respectively. It was observed for Silica NPs-CPE that the surface was 1.22 times greater than that in the bare electrode.

Electrooxidation Behaviors of DCF

Figure 3 shows cyclic voltammograms for the modified and unmodified use of cyclic voltammetry in 0.1 M phosphate buffer solution and pH 7.0 in the presence of

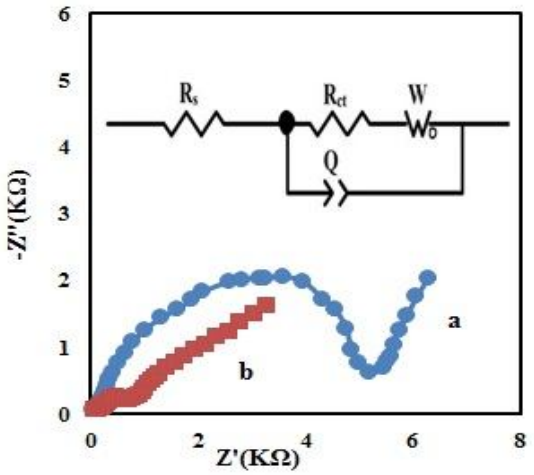

Fig. 1. EIS responses of (a) bare CPE and (b) SilicaNPsCPE electrodes in the presence of 5.0 mM $[Fe\text{-}(CN)_6]^{3-/4-}$ (1:1) in 0.1 M KCl. The inset shows the corresponding equivalent circuit.

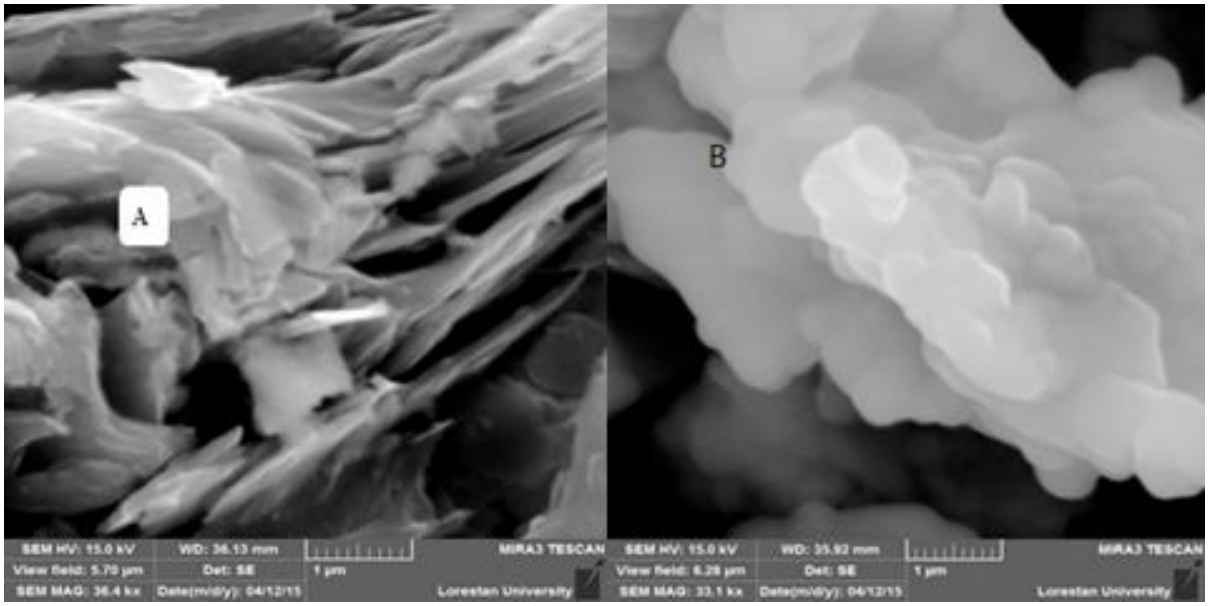

Fig. 2. SEM images of CPE (A), SEM images of SilicaNPsCPE (B).

DCF 0.1 mM (c, d) and in the absence of DCF (a, b). The oxidation peak potential is located at 0.751 V and 0.698 V on the unmodified and modified electrodes (c, d), respectively. The oxidation peak current significantly increases to 14.8 µA, which is 3.3 times higher than that at CPE. The results of the enhancement of peak current and the decrease of the overpotential showed that the presence of Silica nanoparticles leads to the improved electrocatalytic

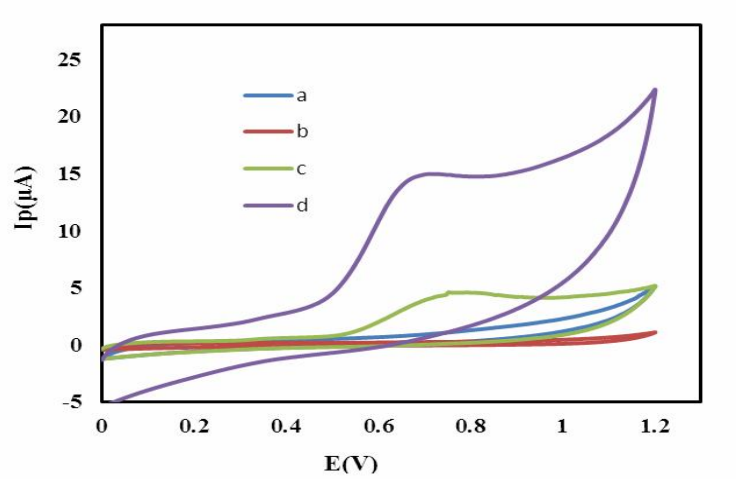

Fig. 3. Cyclic voltammograms obtained for CPE (a, c) and SilicaNPsCPE (b, d) in 0.1M phosphate buffer solution of pH 7.0, Scan rate 0.1 V/s, with (c,d) and without (a,b) addition of 0.1 mM DCF.

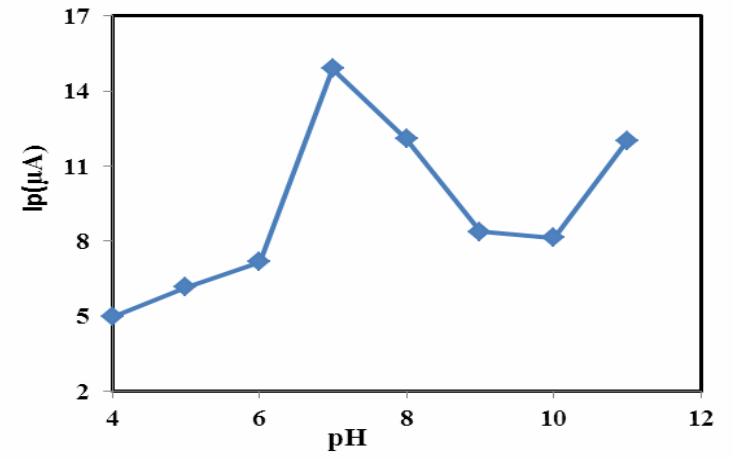

Fig. 4. Influence of pH on peak current in the cyclic voltammograms of 0.1 mM DCF. Measurements carried out at the surface of SilicaNPsCPE in 0.1 M buffered solution with different pH values, 4.0-11.0 at scan rate of 0.1 V s^{-1}.

activity of DCF and to the faster electron transfer at the SilicaNPsCPE. Hence, the SilicaNPsCPE exhibited a catalytic activity for the detection of DCF.

The pH dependency on 1.0 mM DCF at SilicaNPs-CPE was investigated in the various pHs of 4.0-11.0. As shown in Fig. 4, the peak current increased with increase in pH from 4.0-7.0, and then irregularly decreased from 7.0-11.0. Therefore, the best result was obtained at pH 7.0. For this reason, pH 7.0 value of pH was chosen for the subsequent electrochemical experiments.

Effect of Scan Rate

The scan rate effect was examined while the scan rate was increased from 20 to 500 mV/s for 0.1 M DCF in 0.1 M phosphate buffer solution of pH 7.0 (Fig. 5A). The plot of the anodic peak current was dependent linearly on the

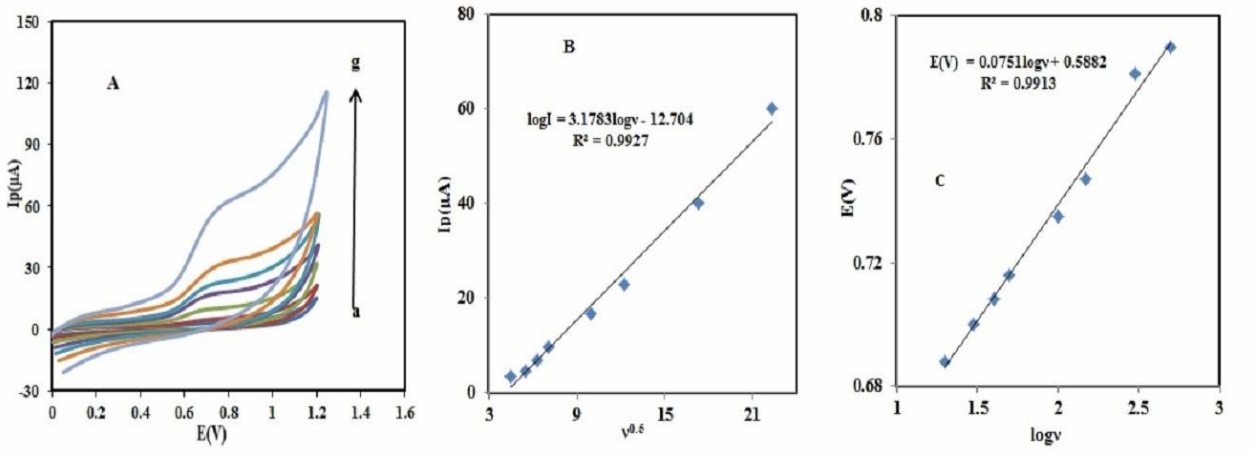

Fig. 5. (A) Cyclic voltammograms of 0.1 mM DCF on the SilicaNPsCPE with different scan rates (a-g: 20, 30, 50, 100, 150, 300 and 500 mV s^{-1}) in pH 7.0 PBS. (B) Redox peak current versus the square root of the scan rate. (C) Variation of Ep versus the logarithm of the scan rate.

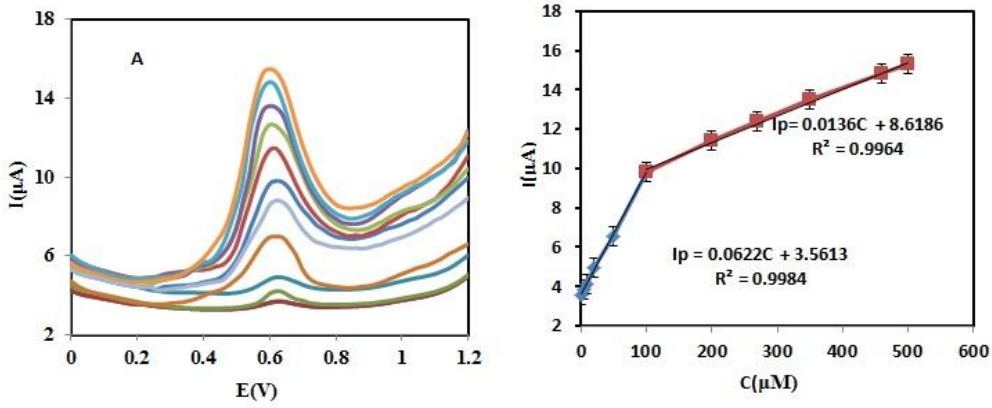

Fig. 6. (A) Differential pulse voltammograms of SilicaNPsCPE in 0.1 M PBS (pH 7.0) containing different concentrations of DCF, from 0.1, 5.0, 8.0, 20.0, 50.0, 80.0, 100.0, 200, 270, 350, 460 and 500.0 µM of DCF. (B) (B) Calibration plot observed for DCF in two linear ranges of 0.1-100.0 and 100.0-500.0 µM.

square root of the sweep rate ($v^{1/2}$), with the coefficients of correlation being 0.9927 for all scan rates (Fig. 5B). This indicates that the nature of redox process is controlled by the diffusion redox process of DCF. In this work, a slope value of 0.0751 V was obtained from the plot of E_p *vs.* logv, (Fig. 5C). For the anodic peaks, the slope of the linear segment is equal to (1 - α)nF. Based on the previous articles published [11], the number of electron transfer for oxidation of DCF was 2. Thus, α_a is 0.6 for two electron transfer process, indicating that the rate control will be the first order step on the basis of the electron transfer.

Calibration Plot and Limit of Detection

Using the DPV technique, the electrooxidation of DCF was studied in 0.1 M phosphate solution pH 7.0 at the surface of SilicaNPsCPE. Results (shown in Fig. 6 A)

Table 1. Comparison of some Electrochemical Methods for the Determination of DCF

Method	Electrode	Linear range	LOD	Ref.
CV	DyNW/CPE[a]	0.01-1.0 μM	5.0 nM	[11]
SWV[b]	SWCNT modified EPPGE[c]	0.02-1.5 μM	0.02 μM	[12]
SWV	EPPG	0.01-1.0 μM	6.2 nM	[13]
DPV	MWCNTs/$Cu(OH)_2$ nanoparticles/IL nanocomposite	0.18-119 μM	0.04 μM	[14]
DPV	TCPE[d]	10.0-140.0 μM	3.28 μM	[15]
DPV	MWCNT-IL/CCE[e]	0.05-50.0 μM	0.018 μM	[16]
DPV	MWCNT-IL/CCE[f]	0.05-20.0 μM	27.0 nM	[17]
DPV	IL/CNTPE[g]	0.50-300.0 μM	0.2 μM	[18]
DPV	DNA-GO/GCE[h]	1.0-130.0 μM	-	[19]
SWV	Pt	1.5-17.5 μg ml^{-1}	0.50	[20]
DPV	Silica NPs/CPE	0.1 -500.0 μM	0.046 μM	This work

[a]Dysprosium nanowire carbon paste electrode. [b]Square wave voltammetry. [c]Edge-plane pyrolytic graphite electrode coated with single wall carbon nanotubes. [d]Tyrosine-modified carbon paste electrode. [e]Multiwalled carbon nanotube and ionic liquidmodified carbon ceramic electrode. [f]Multi-walled carbon nanotubes and an ionic liquid composite. [g]Jonic liquid-modified carbon nanotubes paste electrode. [h]DNA graphene oxide glassy carbon electrode

Table 2. Determination of DCF in Commercially Available Diclofenac Sodium Tablet Samples (n = 3 Replicate Measurements) at SilicaNPsCPE by DPV

Sample	Added (μM)	Found (μM)	t_{Exp}	t_{Tab}	RSD	Recovery (%)
Tablet (50 mg)	50.0	50.2	0.47	4.30	1.46	100.4
	70.0	69.3	0.64	4.30	2.75	99.0
Tablet (25 mg)	30.0	29.4	2.22	4.30	1.58	98.0
	80.0	81.4	0.54	4.30	2.36	101.75

Table 3. Results of Interference Study for on the Determination of 40.0 µM DCF in pH 7.0 at SilicaNPsCPE

Species	Tolerance limits ($C_{Species}/C_{DCF}$)
Ca^{2+}, Na^{+}, Ba^{2+}, Mg^{2+}, K^{+}	1000
Fe^{3+}, Pb^{2+}, Fe^{2+}, Cu^{2+}	200
SO_4^{2-}, CO_3^{2-}, Cl^{-}	1000
Ascorbic acid, Uric acid, Naproxen	100
Glucose, Maltose, Sucrose	500

indicate that the DPVs of DCF oxidation at the surface of the SilicaNPsCPE were linearly dependent on the DCF concentrations, over the range of 0.1-500.0 µM (Fig. 6B). The calibration curve was developed by measuring the peak current by means of the newly optimized DPV parameters. The mean of eight continuous measurements was used for the development of the calibration curve in Fig. 6B.

Results showed that there were linear relationships between the oxidation peak currents and the DCF concentration in two different linear ranges of 0.1-100.0 µM (Ipa = 0.0622 C (µM) + 3.5613) and 100.0-500.0 µM (Ipa = 0.0136 C (µM) + 8.6186), with the correlation coefficients being R^2 = 0.9984 and 0.9964, respectively. The limit of detection was found to be 0.046 µM for the DCF in the lower range region. Table 1 shows a comparison of some electrochemical methods for the determination of sodium diclofenac.

Determination of DCF in Pharmaceutical

The proposed method was applied to the voltammetric determination of DCF in real samples. Table 2 shows the results of the proposed voltammetric method and the label values. The standard addition method can be used for the straightforward evaluation of DCF. Given that the recovery and RSD were acceptable, the proposed methods proved to be a suitable tool for the determination of DCF in pharmaceutical formulations.

As shown in Table 2, the t_{exp} values were calculated based on the t-test [33]. Since t_{exp} is lower than t_{crit} (t_{crit} = 4.30), there is no evidence for any systematic error in the results obtained.

Studies of Interferences

Effects of some coexisting substances on the determination of 40.0 µM DCF were investigated, and the results are shown in Table 3. As it can be seen, few of them disturbed the determination, and the Silica NPs-CPE electrode had satisfactory selectivity toward the DCF determination.

Reproducibility, Repeatability and Stability

To investigate the precision of the determination, the same SilicaNPs-CPE was used for seven parallel determinations of 40.0 µM DCF solutions, and the RSD was determined to be 1.95%. The results indicated that the SilicaNPs-CPE showed good reproducibility. Six SilicaNPs-CPEs were fabricated with the same procedure and were applied to the determination of 40.0 µM DCF with a relative standard deviation of 2.45%, which indicates high reproducibility of the Silica NPs-CPE electrode. The electrochemical sensor showed no obvious decrease in the current response to DCF in the first week and maintained about 95% of its initial value after 1 month, which showed good stability.

CONCLUSIONS

In this research, a new electrochemical sensor was

fabricated on the basis of the nano-Silica carbon paste for the sensitive determination of DCF. The SEM and EIS methods were employed to investigate the characteristics of the Silica nanoparticles modified electrode. This electrode has a number of advantages, such as easy preparation, high stability, reasonable selectivity, fast response time, long-term stability, and applicability over a wide pH range. Moreover, it shows excellent stability, reproducibility, and high sensitivity in real samples.

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