Translating potentiometric detection into non-enzymatic amperometric measurement of H₂O₂

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ABSTRACT

The developments of alternative signal readout strategies for the ion-selective electrodes (ISEs) are necessary in order to break through the limitation of the Nernst equation. In this work, a simple, convenient and easily operated strategy based on the non-enzymatic amperometric measurement of H₂O₂ is proposed to read out the potentiometric responses for the ISEs. The proposed amperometric signal readout based on H₂O₂ is carried out in a two compartment electrochemical cell configuration containing a detection cell and a sample cell, physically connected by a salt bridge. A glassy carbon (GC) electrode is placed in the detection cell to monitor the oxidation current of H₂O₂, and an ISE is placed in the sample cell to act as both the reference electrode and the potentiometric sensor for obtaining the ion activities. The oxidation of H₂O₂ is induced by a constant potential applied between the GC electrode and the ISE, and subsequently modulated by the potential change of the ISE in the presence of the primary ion. The proposed amperometric signal readout based on H₂O₂ shows the satisfied slope sensitivity and detection limit, which are better than or compared to those for the potentiometric responses for the ISEs. This work provides a general strategy for transforming the potential response of the ISEs into the amperometric readout, and is promising for detection of cations (eg., Ca²⁺) and anions (eg., NO₃⁻) with high sensitivity and excellent selectivity.

1. Introduction

As an important branch in the electrochemical sensors, the traditional potentiometric ion-selective electrodes (ISEs) are usually detected under the zero current condition through a two-electrode system [1], including an indicator electrode and a reference electrode, and the ion activity can be obtained based on the observed potential according to the Nernst equation. For these reasons, ISEs show some unique characteristics as compared to other electrochemical sensors, such as providing the thermodynamic information (i.e. ion activity), ease of operation, low energy consumption and portability.

In recent years, with the introduction of the new sensing concepts and the instrumental control [2], ISEs have been expanded to be measured under the control of the applied current or potential through a

three-electrode system [3], such as thin-layer coulometry [4], chronopotentiometry/galvanostatic polarization [5–9], thin-layer ion transfer voltammetry [10,11], and constant potential coulometry [12]. Meanwhile, the corresponding signal readout strategies, such as coulometric charge [13,14], transition time [15], and voltammetric current [16,17], have been proposed based on the ISEs as the working electrodes. In fact, the studies about the application of the ISEs as the reference electrodes in modulating the potential of the working electrodes have also attracted some attentions. For example, Bakker's group reported an electrogenerated chemiluminescence (ECL) readout for the potentiometric sensors, which applied the change in the ion concentration to control both the potential response of the ISE and the ECL intensity [18,19]. Qin's group developed an optical ion sensing platform for the ISEs, which employed the ISEs to modulate the release of

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Fig. 1. Schematic representation of the detection principle for translating potentiometric detection into non-enzymatic amperometric measurement of H_2O_2 .

enzyme and produce a visual color change [20]. Moreover, the photoelectric current is also proposed for reading out the potential response through the control of the photoactive material by using an ISE [21]. These reported methods provide versatile signal readouts based on the ISEs as the reference electrodes. However, these reported signal readout systems depend on the complicated instruments, or need the tedious operation steps, which may restrict their wide applications. Therefore, a simple, convenient and easily operated strategy for obtaining alternative readout for the ISEs needs to be further investigated.

Different from the traditional potentiometric response with mV grade, amperometry can be measured at the pA level, which is more sensitive to detect the small concentration changes of the primary ion [22]. Hydrogen peroxide (H_2O_2) is an important metabolic product of the living organisms [23], and it is also a byproduct of oxidases enzyme-catalyzed reactions [24]. In recent years, the non-enzymatic amperometric measurement plays a promising role in sensitive and selective detection of H_2O_2 as compared to the enzymatic electrochemical sensors [25], which avoids the immobilization of enzyme and the rigorous preservation conditions.

Herein, the amperometric signal readout for the ISEs is proposed based on the non-enzymatic measurement of H_2O_2 . The mechanism is that the oxidation current for H_2O_2 is modulated by an ISE acting as the reference electrode. By using Ca^{2+} and NO_3^- as the cationic and anionic models, the transformation from the potentiometric detection to the non-enzymatic amperometric measurement of H_2O_2 is shown.

2. Experimental

2.1. Reagents and materials

N, N, N', N'-Tetracyclohexyl-3-oxapentanediamide (Ca^{2+} ionophore II, ETH 129), tridodecylmethylammonium nitrate (TDMA- NO_3^-), sodium tetrakis[3, 5-bis(trifluoromethyl)phenyl]borate (NaTFPB), tetradodecylammonium tetrakis(4-chlorophenyl)borate (ETH 500), 2-nitrophenyl octyl ether (o-NPOE), bis(2-ethylhexyl)sebacate (DOS), and poly(vinyl chloride) (PVC) were obtained from Sigma-Aldrich. Ordered mesoporous carbon (OMC) with an average pore diameter of 3.8–4 nm and a BET surface area of $\geq 900 \text{ m}^2/\text{g}$ was purchased from Nanjing XFNANO Material Tech Co., Ltd. Tetrahydrofuran (THF), hydrogen peroxide (H_2O_2 , 30 wt%) and other chemicals reagents with analytical grade were obtained from Sinopharm Chemical Reagent Co., Ltd. THF was freshly distilled prior to use throughout the experiment. Deionized (DI) water ($18.2 \text{ M}\Omega \text{ cm}$ specific resistance) was obtained with a Pall Cascada

laboratory water system to prepare all of the solutions.

2.2. Fabrication of the solid-contact Ca^{2+} and NO_3^- -ISEs

The glassy carbon (GC) disk electrode with the diameter of 3 mm was carefully polished with $0.05 \mu\text{m}$ Al_2O_3 slurry, and then cleaned with ethanol and deionized water under the ultrasonic condition for 2 min, respectively. The OMC suspension (3 mg/mL) was prepared according to the reported literature [26], and then drop cast on the polished GC electrode. After being dried at room temperature, the GC electrode modified with OMC as solid contact (GC/OMC) was obtained for further use.

For preparing the solid-contact Ca^{2+} -ISE, the Ca^{2+} -selective membrane components (totaling 180 mg) containing 2.3 wt% ETH 129, 2.4 wt% NaTFPB, 31.8 wt% PVC and 63.5 wt% o-NPOE, were dissolved in 2 mL THF through stirring for 2 h. Then, 90 μL of the membrane cocktail was drop cast on the above GC/OMC electrode. Finally, the GC/OMC/ Ca^{2+} -ISE was prepared after being dried at room temperature. The GC/OMC/ NO_3^- -ISE was fabricated by the same procedure, and the NO_3^- -selective membrane cocktail contains 100 mg of 1 wt% TDMA- NO_3^- , 1 wt% ETH 500, 32.7 wt% PVC and 65.3 wt% DOS, and 1 mL of THF. For further use, the prepared GC/OMC/ Ca^{2+} -ISE and GC/OMC/ NO_3^- -ISE were conditioned in $1.0 \times 10^{-3} \text{ M}$ CaCl_2 and NaNO_3 overnight, respectively.

2.3. Apparatus and measurements

Potentiometric measurements were carried out in two ways by using a 16 channel potentiometer (EMF 16, Lawson Labs, Inc) at room temperature. One way is performed with an Ag/AgCl (3 M KCl) electrode as the reference electrode in the galvanic cell: Ag/AgCl (3 M KCl)/sample solution/ Ca^{2+} or NO_3^- -selective membrane/OMC/GC electrode, and another way is carried out with a GC electrode as the indicator electrode and the prepared GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE as the reference electrode. The liquid junction potentials were calculated by the Henderson equation, and the ion activities were obtained by the Debye-Hückel equation.

Cyclic voltammetry (CV) and multi-potential step technique were performed in a 0.1 M PBS buffer solution (pH 7.2) by using a CHI 760D electrochemical workstation (Shanghai Chenhua Apparatus Corporation, Shanghai, China) with a three-electrode system containing a bare GC working electrode, an Ag/AgCl (3 M KCl) reference electrode and a platinum wire-based auxiliary electrode in the potential range of 0–1.0

Fig. 2. Cyclic voltammograms for the bare GC electrode in the 0.1 M PBS buffer solution (pH 7.2) in the absence and presence of 30 mM H_2O_2 (a), and multi-potential step curve for 30 mM H_2O_2 recorded in the 0.1 M PBS buffer solution (pH 7.2) under the different applied potentials (b). Inset: the curve for the oxidation current of H_2O_2 vs. the applied potential.

V with a scan rate of 0.1 V/s.

Chronoamperometric measurement was carried out under stirring in a two compartment electrochemical cell configuration containing a detection cell and a sample cell. The bare GC electrode and a platinum wire were placed in the detection cell, and an Ag/AgCl (3 M KCl) reference electrode or the GC/OMC/ Ca^{2+} -ISE or the GC/OMC/ NO_3^- -ISE was placed in the sample cell. The background solutions for the two cells are successively 0.1 M PBS buffer solution (pH 7.2), and 1.0×10^{-2} M NaCl for Ca^{2+} or deionized water for NO_3^- , respectively. These two cells were connected by a salt bridge containing 1 g of agar, 10 g of KCl and 33 mL of ultrapure water. The real-time change in the oxidation current of H_2O_2 with a constant concentration was recorded and modulated by the GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE acting as the reference electrode. The current change ($\Delta I = I - I_0$) was used for quantifications through the difference between the baseline and the measured current.

3. Results and discussion

3.1. Detection principle

The detection principle for translating the potentiometric detection into non-enzymatic amperometric measurement of H_2O_2 is shown in Fig. 1. A bare GC electrode acts as the working electrode, while the GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE is used not only as the reference electrode, but also as the potentiometric sensor for obtaining the activities of Ca^{2+} or NO_3^- . The working electrode and the ISE-based reference electrode are separately placed in the two electrochemical

cells in order to avoid the mutual interfering from the different background solutions, and a salt bridge is used to connect these cells. During the measurements, a certain constant potential is applied between the GC electrode and the GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE, which would induce the oxidation of H_2O_2 . As the addition of the solution containing Ca^{2+} or NO_3^- in the sample cell, the potential of the GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE as the reference electrode will be changed, which subsequently influence the oxidation current of H_2O_2 under the constant applied potential in the detection cell. Therefore, the transformation from the potential response of the ISE to the amperometric readout is developed. The corresponding theoretical mechanism for the amperometric signal readout based on H_2O_2 for the ISEs is speculated according to the Butler-Volmer equation [27]. As shown in the theoretical model in supporting information, the relationship between the current based on H_2O_2 and the ion activity for the ISE is exponentially dependent (see equation 5 in supporting information).

3.2. Electrochemical characterization of H_2O_2

It's known that many nanomaterials have been reported to improve the sensitivity for the non-enzymatic amperometric measurements of H_2O_2 [28–31]. However, in this work, the aim is to demonstrate the proposal for the transformation between the potential response of the ISE and the amperometric signal readout, rather than obtaining the high sensitive detection of H_2O_2 . Therefore, the bare GC electrode was just chose for the further work. As shown in Fig. 2a, there is a clear oxidation current in the presence of H_2O_2 , indicating that the bare GC electrode is

Fig. 3. Time-dependent potential response traces for the GC working electrodes obtained by the GC/OMC/ Ca^{2+} -ISE (a) and the GC/OMC/ NO_3^- -ISE (b) as the reference electrodes, respectively.

Fig. 4. Time-dependent amperometric signal readout based H_2O_2 (a) and the corresponding calibration curve (b) for the GC/OMC/ Ca^{2+} -ISE, the potentiometric calibration curve for the GC/OMC/ Ca^{2+} -ISE (c), and influence of NaCl on the amperometric signal for the GC/OMC/ Ca^{2+} -ISE (d). The applied potential is 0.8 V, and the concentration of H_2O_2 is 30 mM. The letters, a-r, refers to the concentrations for Ca^{2+} are 1.0×10^{-7} , 1.0×10^{-6} , 2.0×10^{-6} , 5.0×10^{-6} , 8.0×10^{-6} , 1.0×10^{-5} , 2.0×10^{-5} , 5.0×10^{-5} , 8.0×10^{-5} , 1.0×10^{-4} , 2.0×10^{-4} , 5.0×10^{-4} , 8.0×10^{-4} , 1.0×10^{-3} , 2.0×10^{-3} , 5.0×10^{-3} , 8.0×10^{-3} and $1.0 \times 10^{-2} \text{ M}$, respectively.

feasible for detecting H_2O_2 . The influence of the applied potentials on the oxidation currents of H_2O_2 were investigated by using the multi-potential step technique. As shown in Fig. 2b, the oxidation currents of H_2O_2 increase as the increase in the applied constant potentials, which indicates that the high potential is favorable for the oxidation of H_2O_2 . Additionally, the changes in oxidation currents of H_2O_2 , caused by 2 mV change in the applied potential, are found to be more than dozens of nA (Fig. S1a). This result indicates the high sensitivity for the amperometric signal of H_2O_2 , which is favorable for modulating the oxidation current of H_2O_2 by using an ISE as the reference electrode. Moreover, the calibration curve for detection of H_2O_2 by using the bare glassy carbon electrode is measured (Fig. S1b), and 30 mM H_2O_2 in the linear range of 1–38 mM ($n = 3$, $R = 0.9926$) was chose for further use.

3.3. Amperometric signal performances based on H_2O_2 for the ISEs

In order to obtain the relationship between the potential response of the ISE to the amperometric signal of H_2O_2 , the two compartment electrochemical cell is used, in which the GC working electrode and the reference electrode based on the GC/OMC/ Ca^{2+} -ISE or the GC/OMC/ NO_3^- -ISE are separately placed. The potentiometric performance based on these two cells was initially investigated under the zero current condition. As shown in Fig. 3a, the potential of the GC electrode is found to be decreased as the increase in the concentration of Ca^{2+} , which is contrary to that for the GC/OMC/ Ca^{2+} -ISE as the working electrode with Ag/AgCl (3 M KCl) as the reference electrode (Fig. S2). Similar results are also found for the GC/OMC/ NO_3^- -ISE as the reference electrode (Fig. 3b and S3). These results indicate that the potential for the GC electrode can be modulated by the GC/OMC/ Ca^{2+} -ISE or GC/OMC/ NO_3^- -ISE. Moreover, the potential stabilities for the proposed ISEs as both of the reference electrode and the indicator electrode were also

investigated under the zero current conditions, respectively. As shown in Fig. S4, the GC/OMC/ Ca^{2+} -ISE and GC/OMC/ NO_3^- -ISE as the reference electrodes show good potential stabilities, which are comparable to those for the indicator electrodes.

The applied potential between the GC electrode and the ISE-based reference electrode was also optimized. As shown in Fig. S5a, when the GC/OMC/ Ca^{2+} -ISE was used as the reference electrode, the addition of H_2O_2 in the 0.1 M PBS buffer solution (pH 7.2) causes an obvious current change under the constant potential condition, due to the oxidation of H_2O_2 . Moreover, as the increase in the applied potentials, the oxidation currents of H_2O_2 are found to be increased. However, the apparent drift is also observed when the applied potential is more than 0.8 V. Similarly results are also found by using the GC/OMC/ NO_3^- -ISE as the reference electrode (Fig. S5b). The reason is speculated to be that too high overpotential is unfavour for obtaining the stable oxidation current of H_2O_2 . Additionally, although there is a stable oxidation current under the applied potential of 0.75V, the current value is smaller than that under the applied potential of 0.8 V. Therefore, considering the further resolution for the amperometric signal readout based H_2O_2 , 0.8 V, which would be applied between the GC electrode and the ISE-based reference electrode, was selected for further use.

The amperometric signal readout based on H_2O_2 for the GC/OMC/ Ca^{2+} -ISE was investigated under the control of the applied potential. As shown in Fig. 4a, the oxidation currents of H_2O_2 , which are modulated by the GC/OMC/ Ca^{2+} -ISE as the reference electrode, are found to be increased as the increase in the concentrations of Ca^{2+} . Additionally, the calibration curve for the GC/OMC/ Ca^{2+} -ISE based on amperometric signal of H_2O_2 is shown in Fig. 4b. It's found that there are two linear responses in the concentration range of $5.0 \times 10^{-6} - 1.0 \times 10^{-4} \text{ M}$ and $1.0 \times 10^{-4} - 1.0 \times 10^{-2} \text{ M}$. The corresponding linear equations between the current change and logarithmic of the activity of Ca^{2+} are shown as

Fig. 5. Time-dependent amperometric signal readout based H₂O₂ (a) and the corresponding calibration curve (b) for the GC/OMC/NO₃-ISE, the potentiometric calibration curve for the GC/OMC/NO₃-ISE (c), and influence of NaCl on the amperometric signal for the GC/OMC/NO₃-ISE. The applied potential is 0.8 V, and the concentration of H₂O₂ is 30 mM. The letters, a-n, refers to the concentrations for NO₃⁻ are 1.0×10^{-7} , 1.0×10^{-6} , 2.0×10^{-6} , 5.0×10^{-6} , 8.0×10^{-6} , 1.0×10^{-5} , 2.0×10^{-5} , 5.0×10^{-5} , 8.0×10^{-5} , 1.0×10^{-4} , 2.0×10^{-4} , 5.0×10^{-4} , 8.0×10^{-4} and 1.0×10^{-3} M, respectively.

follows: $\Delta I = 3.58 \log a_{\text{Ca}^{2+}} + 20.06$ ($n = 3$, $R = 0.9959$) and $\Delta I = 7.20 \log a_{\text{Ca}^{2+}} + 34.17$ ($n = 3$, $R = 0.9941$). These phenomena may be attributed to the fact that the oxidation current for H₂O₂ is not linearly dependent on the applied current (Fig. 2b). The detection limit for measuring Ca²⁺ based on the amperometric signal of H₂O₂ is calculated to be 1.1×10^{-6} M ($3\sigma/s$), which is comparable to the detection limit of 1.3×10^{-6} M calculated as the intersection of the two slope lines for the potential response of the GC/OMC/Ca²⁺-ISE in the linear range of 5.0×10^{-6} – 1.0×10^{-2} M with the slope of 25.4 mV/dec under the zero current condition ($n = 3$, $R = 0.9996$) (Fig. 4c). In addition, from the linear equations, it can be estimated that the oxidation current change of H₂O₂, caused by 10% change in the activity of Ca²⁺, is up to hundreds of nA, which indicates the high slope sensitivity for the amperometric signal readout as compared to the potentiometric response. Moreover, the selectivity of the amperometric signal readout based on H₂O₂ for the GC/OMC/Ca²⁺-ISE was also investigated. As shown in Fig. 4d, the amperometric signal is not influenced by the addition of NaCl, which may be attributed to the excellent selectivity toward Na⁺ for the Ca²⁺-selective membrane [32]. Additionally, the reversibility for the amperometric signal readout based on H₂O₂ for the GC/OMC/Ca²⁺-ISE was also investigated through the dilution method (Fig. S6), and it's found that the amperometric signal readout for detection of Ca²⁺ shows good reversibility.

The amperometric signal readout based on H₂O₂ for the GC/OMC/NO₃-ISE was also measured. It can be seen that the oxidation currents of H₂O₂ are decreased as the increase in the concentrations of NO₃⁻ (Fig. 5a), and the two linear ranges are obtained from 5.0×10^{-6} to 1.0×10^{-4} M and from 1.0×10^{-4} to 1.0×10^{-3} M (Fig. 5b), respectively. The corresponding linear equations between the current change and logarithmic of the activity of NO₃⁻ are shown as follows: $\Delta I = -1.12 \log a_{\text{NO}_3^-} - 6.48$ ($n = 3$, $R = 0.9992$) and $\Delta I = -0.64 \log a_{\text{NO}_3^-} - 4.57$ ($n = 3$,

Table 1

Comparisons of the results for detection of Ca²⁺ and NO₃⁻ in mineral water samples by using the amperometric signal readout based on H₂O₂ and the potential response for the GC/OMC/Ca²⁺-ISE and the GC/OMC/NO₃-ISE, respectively.

Sample	Ca ²⁺ ($\times 10^{-5}$ M)		NO ₃ ⁻ ($\times 10^{-5}$ M)	
	Amperometric signal	Potential response	Amperometric signal	Potential response
1	33.42 ± 1.56	33.09 ± 2.75	2.59 ± 0.17	2.13 ± 0.19
2	17.38 ± 1.09	16.73 ± 3.96	2.52 ± 0.23	2.89 ± 0.25
3	163.13 ± 2.72	163.66 ± 3.07	3.00 ± 0.07	2.37 ± 0.14
4	6.10 ± 0.94	6.20 ± 1.24	3.53 ± 0.12	3.46 ± 0.13

$R = 0.9945$). The detection limit for the measurement of NO₃⁻ based on the amperometric signal of H₂O₂ is calculated to be 3.2×10^{-6} M ($3\sigma/s$), which is compared to the detection limit of 2.5×10^{-6} M calculated as the intersection of the two slope lines for the potential response of the GC/OMC/NO₃-ISE in the linear range of 5.0×10^{-6} – 1.0×10^{-3} M with the slope of -55.3 mV/dec ($n = 3$, $R = 0.9991$) (Fig. 5c). Additionally, it's found that the amperometric signal of H₂O₂ for the GC/OMC/NO₃-ISE is decreased as the addition of NaCl (Fig. 5d), which is similar to that for the potential response of the GC/OMC/NO₃-ISE in the presence of Cl⁻ with high concentrations under the zero-current condition [26]. This phenomenon may be due to the limited selectivity of the NO₃⁻-selective membrane toward Cl⁻ ($\log K_{\text{NO}_3^-, \text{Cl}^-} = -2.0$) [26], which is quite different from the selectivity for the Ca²⁺-selective membrane toward Na⁺ ($\log K_{\text{Ca}^{2+}, \text{Na}^+} = -8.3$) [32]. This result also indicates that the amperometric signal of H₂O₂ for the GC/OMC/NO₃-ISE is dependent on the inherent selectivity of the NO₃⁻-selective membrane.

3.4. Practical applications

The analytical applications of the proposed amperometric signal readout based on H_2O_2 for the GC/OMC/ Ca^{2+} -ISE and the GC/OMC/ NO_3^- -ISE were investigated, and the concentrations of Ca^{2+} and NO_3^- in mineral water samples were measured by the proposed amperometric signal of H_2O_2 and the potentiometric responses through the standard addition method, respectively. As shown in Table 1, the concentrations for Ca^{2+} and NO_3^- obtained by the amperometric signal readout based on H_2O_2 are found to agree well with those detected by the potentiometric responses for the ISEs, while the standard deviations for the amperometric signals are smaller than those for the potential responses of the proposed ISEs. These results indicate that the transformation from the potential response for the ISEs to the amperometric readout is feasible and reliable, but also the proposed amperometric signal readout based on H_2O_2 shows better or compared to resolution than those for the potential response of the ISEs.

4. Conclusions

This work developed the amperometric signal readout based on the non-enzymatic measurement of H_2O_2 for the ISEs. This proposed readout strategy for the ISEs is simple, convenient, low cost and easy operation as compared to other optical readout. Although the proposed amperometric signal readout based on H_2O_2 for the ISEs shows the two linear responses, the slope sensitivity and the detection limit are better than or compared to those for the potentiometric response. Moreover, the selectivity for the proposed amperometric signal based on H_2O_2 is found to depend on the inherent properties of the ion-selective membrane. The transformation from the potential response for the ISEs to the amperometric readout based on H_2O_2 is promising for detection of cations and anions with both high sensitivity and high selectivity.

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.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.talanta.2021.122489>.

Credit author statement

Tanji Yin: Conceptualization; Methodology; Validation; Formal analysis; Investigation; Resources; Data curation; Writing – original draft; Writing – review & editing; Visualization; Supervision; Project administration; Funding acquisition, Hemin Wang: Methodology; Validation; Investigation; Data curation; Writing – original draft; Writing – review & editing. Jinghui Li: Methodology; Validation; Investigation. Baiqing Yuan: Writing – review & editing; Supervision., Wei Qin: Formal analysis; Resources; Writing – review & editing; Visualization; Project administration; Funding acquisition.

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