Synthesis of copper–nitrogen codoped carbon quantum dots using frangipani as a carbon source and application of metronidazole determination

Yuwei Lan1 · Wenbin Bao1 · Chunfeng Liang1 · Guowei Li1 · Liya Zhou1 · Jiachu Yang1 · Liubai Wei1 · Qionghua Su1

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Abstract
High-fluorescence Cu/N-codoped carbon quantum dots (Cu/NCQDs) were prepared by a one-step hydrothermal method using frangipani and copper acetate hydrate. The prepared Cu/NCQDs exhibited a nearly spherical morphology, and the average particle size was 2.58 nm. The surface of the Cu/NCQDs contains abundant hydrophilic groups –OH, –NH2 and –COOH, which explains their high water solubility. The Cu/NCQDs exhibited high-intensity, stable blue fluorescence that is independent of the excitation wavelength. As metronidazole can effectively quench the fluorescence intensity of Cu/NCQDs, a metronidazole fluorescence-detection method using Cu/NCQDs as the fluorescence probe was developed, and the quenching mechanism was studied. The method has the advantages of simplicity, speed, and low cost. Besides, the linear equation was \( F = -3.235 + 9.064C_{\text{MNZ}}(\mu\text{mol/L}) \), the correlation coefficient \( (R^2) \) was 0.996, and the detection limit was 0.28 \( \mu\text{mol/L} \). Further, the metronidazole content in actual samples was determined using this method; the recovery rates of the metronidazole tablets and honey samples were 96.8–103.7%, and relative standard deviation was lower than 6%.

Keywords Cu/NCQDs · Fluorescence · Metronidazole · Fluorescence probe

Introduction
Metronidazole (2-methyl-5-nitro-1H-imidazol-1-ethanol, MNZ), a 5-nitroimidazole antibiotic, is used to treat or prevent systemic or local infectious diseases caused by anaerobic bacteria and protozoa, such as lower respiratory, female genital tract, and digestive tract infections. In animal husbandry, metronidazole is often used as a feed or drug additive to promote the growth of pigs, cattle, and sheep and to inhibit the growth of parasites (Hu et al. 2020; Liu Dan 2019; Haddao 2018). However, studies have shown that metronidazole has teratogenic effects on animal and plant cells, including carcinogenic and mutagenic effects. If used irrationally or abused in livestock and poultry feed, metronidazole residues may persist in animal tissue and could be transmitted through the food chain, thereby indirectly causing damage to the human body, such as epileptic neuropathy (Xiaojiao 2021; Bilici et al. 2018). As is well known, the abuse of antibiotics, release of antibiotics into the environment, and development of drug-resistant genes in natural ecosystems are increasingly serious global threats. Therefore, the establishment of a rapid and effective metronidazole detection is crucial in ensuring food safety.

Thus far, high-performance liquid chromatography (Zhang 2019; Yang Chunmei 2019), ultra-high-performance liquid chromatography–tandem mass spectrometry (Zhou Yibing 2017; Gao Hegang et al. 2017; Lei et al. 2018), electrochemical method (Haiyan Lei 2018; Li Meina 2019), chemiluminescence (Chu 2021), and other analytical methods have been widely used to detect metronidazole. In particular, the fluorescence-detection method based on carbon quantum dots (CQDs) is promising because of its low cost and simple operation.

CQDs are novel carbon nanomaterials that exhibit photoluminescence (PL) and fluorescence properties. However, pure CQDs, because of the few functional groups on their surfaces, exhibit a low quantum yield (QY), which limits their practical application (Zhang 2019). Studies have shown that surface functionalization and chemical heteroatomic doping are effective methods for improving the fluorescence...
properties of CQDs and expanding their application range (Su 2018). In this regard, N, P, S, B, Cl, and other nonmetallic heteroatoms have been extensively used as dopants for the single doping or codoping of CQDs. In particular, when CQDs are doped with N, whose atomic radius and valence electron structure are similar to those of C, the surface of the CQDs becomes positively charged, which substantially improves not only the interaction between the target analyte and CQDs, but also the QY of the CQDs (Lei 2021). Therefore, many studies on the heteroatom doping of CQDs have used the N atom as the dopant (Liang 2019; PF Fan 2021; Li Quan 2020). However, compared with nonmetal impurity atoms, metal ions, particularly transition metal ions, have more volatile electronics and do not occupy orbits; further, they have larger atomic radii than nonmetallic atoms (Zhang 2019). Thus, transition metal atoms can change the surface charge density of CQDs, which is more advantageous. Recently, the research on the metal-atom doping of CQDs has developed rapidly. Metal atoms, including Cu, Fe, Zn and Mn, have been extensively used (Su 2018; Li et al. 2020). Among them, Cu is widely used in the doping of CQDs because of its safety. Additionally, it facilitates the interaction between aminocarboxyl and hydroxyl groups on the surfaces of CQDs (Liu et al. 2020). Moreover, the Cu atoms doped on the surface of CQDs can form coordination complexes with most small molecules, i.e., chelation, which is essential for the detection of analytes in the environment.

Therefore, high-fluorescence Cu/N-codoped CQDs (Cu/NCQDs) were prepared by one-step hydrothermal method using fractions as carbon source and copper acetate hydrate as copper source. Cu/NCQDs showed strong blue light and excitation independent fluorescence properties. As metronidazole can effectively quench the fluorescence intensity of Cu/NCQDs, a metronidazole fluorescence-detection method using Cu/NCQDs as the fluorescence probe was developed, and the quenching mechanism was studied. The metronidazole content in actual samples was detected using this method, and good results were obtained. The related process is shown in Fig. 1.

### Experimental

#### Materials

Frangipani, ethylenediamine (C\(_2\)H\(_8\)N\(_2\)), acetone (C\(_3\)H\(_6\)O), copper acetate hydrate (Cu (CH\(_3\)COO)\(_2\)·H\(_2\)O), Metronidazole (C\(_4\)H\(_8\)N\(_3\)O\(_3\)), citric acid (C\(_6\)H\(_8\)C\(_6\)), monopotassium phosphate (NaH\(_2\)PO\(_4\)), potassium chloride (KCl), glucose (C\(_6\)H\(_12\)O\(_6\)), ascorbic acid (C\(_6\)H\(_8\)O\(_6\)), saccharose (C\(_12\)H\(_22\)O\(_11\)), beta cyclodextrin (C\(_42\)H\(_70\)O\(_35\)), L-cysteine (C\(_3\)H\(_7\)NO\(_2\)S), magnesium nitrate (Mg (NO\(_3\))\(_2\)), ammonium chloride (NH\(_4\)Cl), calcium chloride (CaCl\(_2\)), sodium carbonate (Na\(_2\)CO\(_3\)).

All drugs were analytically pure, and distilled water was used in the experiment without further purification.

#### Instruments

Electro-thermostatic blast oven (DHG-9146A), UV–VIS spectrophotometer (UV-1800), Fluorospectrophotometer (RF-5301), TEM (TECNAL G2 F30), Fourier Infrared Spectrometer (Nicolet iS50), XPS (ESCALAB 250Xi), Fluorescence Lifetime Spectrometer (FLs980), Centrifuge (H1850).
Preparation of Cu/NCQDs

The specific preparation method of CQDs is as follows: 1.0 g of frangipani powder was dispersed in 40 mL of deionized water. Subsequently, 0.15 g copper acetate hydrate was dissolved in the above solution. After ultrasonic treatment for 10 min, the mixed solution was transferred into a 50 mL high-pressure reaction kettle and placed in an electric thermostatic air blow-drying oven at the temperature of 200 °C. Thereafter, the reaction kettle was cooled naturally to room temperature, and the reaction solution was pumped and filtered. The filtrate was centrifuged at 4000 rpm for 10 min, and the supernatant was filtered again using a water-soluble filter membrane (pore size: 0.22 μm) to obtain the purified fluorescent Cu/NCQD solution. The prepared CQDs solution was stored in refrigerator for later use. Using the same preparation, except the addition of copper acetate hydrate, N-doped CQDs (NCQDs) were prepared as contrast materials.

Quantum yield (QY)

Based on the fluorescence QY of quinine sulfate at 313 nm excitation wavelength of 0.54, the fluorescence yield of the carbon quantum dots was calculated to be 13.6% (NCQDs) and 19.3% (Cu/NCQD). The calculation formula is as follows:

\[ \Phi = \Phi_R \times \frac{A_R}{A} \times \left( \frac{n}{n_R} \right)^2 \]  

(1)

\( R \): quinine sulfate; \( \Phi \): QY; \( A \): absorption intensity of light; \( I \): fluorescence integral intensity; \( n \): represents refractive index. The absorbance of the two solutions was less than 0.1.

Fluorescence detection of metronidazole

The Cu/NCQD standard metronidazole (MNZ) solutions (100 μL) of different concentrations were poured into a series of 10 mL test tubes and diluted to 10 mL using a citric acid sodium dihydrogen phosphate buffer (pH = 4; 0.2 mol/L). After shaking, the solution was stable for 3 min, and the fluorescence spectrum was recorded. The fluorescence intensities with and without the MNZ solution were denoted as \( F \) and \( F_0 \), respectively.

Preparation of honey samples

Metronidazole tablets (0.2 g each) and honey were purchased from Ali Health Pharmacy (Nanning, China). Each metronidazole tablet was ground into powder using an agate mortar, dissolved in distilled water, ultrasonicated for 15 min, and dissolved in a 100 mL volumetric bottle for subsequent analysis. The specific method for pretreating the honey was obtained from the literature (Lei 2018), as follows: 10 mg of the honey sample was dissolved in 1 mL of an acetone solution (5%). After 15 min of ultrasonic treatment, 1 mL of the sample solution was poured into a 10 mL test tube, and 100 μL of the Cu/NCQD solution was added. Afterward, the solution was diluted to scale with the citric acid sodium dihydrogen phosphate buffer (pH = 4).

Results and discussion

**Morphology and structure characterization of the Cu/NCQDs**

The morphology and size of the Cu/NCQDs were determined used transmission electron microscopy (TEM). The results are shown in Fig. 2. As shown in Fig. 2a, the prepared Cu/NCQDs exhibited a nearly spherical morphology and good dispersion in water. Figure 2b shows the particle-size distribution of the Cu/NCQDs. Statistically, the particle-size range of Cu/NCQDs is 1.90–3.70 nm, and the Gaussian fitting curve shows that the average particle size is 2.58 nm.

Figure 2c shows the FT-IR spectra of the NCQDs and Cu/NCQDs, which are exploited to characterize the functional groups on the surface of the CQDs. In Fig. 2c, a wide absorption band can be observed near 3428 cm\(^{-1}\), and the \(-\text{NH}/\text{OH}\) stretching vibration of the Cu/NCQDs (Liu et al. 2020). The absorption peaks slightly lower than 3000 and 1384 cm\(^{-1}\) correspond to the stretching vibration and bending vibration of the alkyl \(\text{C–H}\) bond, respectively. The peak near 1710 cm\(^{-1}\) is assigned to the carbonyl group \(\text{C=O}\), and it is a carboxylic acid in the form of a dimer, which correspond to the asymmetrical stretching vibration of the COOH. The absorption peaks at 1000–1217 cm\(^{-1}\) correspond to the symmetric and asymmetric stretching vibrations of carbon and oxygen compounds (C–O–C), respectively (Liu et al. 2020). The above results indicate the abundance of hydrophilic groups (–OH, –NH\(_2\), and –COOH) on the surface of the Cu/NCQDs, which explains their high water solubility. Further, the hydrophilic groups facilitate the chelation of Cu/NCQDs with Cu\(^{2+}\), as well as promote the surface passivation of the CQDs and Cu doping. Notably, the 870–1000 cm\(^{-1}\) range is denoted as the metal-sensitive region (Liu 2020; Ma 2017; Si et al. 2022). Different from the NCQDs, the Cu/NCQDs exhibited partial absorption in the metal-sensitive region. This is related to the stretching vibration of the N–Cu–N bond and confirms the formation of a Cu coordination complex in the Cu/NCQDs. The FT-IR spectra showed that N and Cu were successfully doped on the surface or the Cu/NCQDs in the form of related groups.
X-ray photoelectron spectroscopy (XPS) was conducted to further confirm the structural composition of the Cu/NCQDs. In the XPS full-scan spectra of the Cu/NCQDs (Fig. 2d), four peaks are observed at binding energies of 284.82, 399.98, 531.32 eV and 932.66 eV, belonging to C 1s, N 1s, O 1s, and Cu 2p, respectively. The C 1s high-resolution spectrum (Fig. 3a) shows four peaks at 284.55, 285.94, 287.11, and 288.10 eV, indicating the existence of carbon in four states: C–C/C=C, C–N/C–O, C=O and COO– (Su 2018), respectively. Figure 3b shows the high-resolution spectrum of O 1s, and the peaks at 530.99 and 532.09 eV correspond to the C=O and C–OH/C–O–C bonds (Fan 2021; Wan 2019), respectively. The N 1s high-resolution spectrum (Fig. 3c) confirmed the presence of C–N–C (399.72 eV), N–C3 (400.59 eV), and N–H bonds (401.87 eV) (Li 2018; Ma et al. 2017). The Cu 2p spectra (Fig. 3d) show two peaks at 933.0 eV and 952.50 eV, attributable to Cu 2p 3/2 and Cu 2p 1/2, respectively, indicative of the N–Cu–N covalent bond in porphyrin–metal complexes. In conclusion, the XPS results are consistent with the FT-IR spectroscopies, which proves that Cu and N were successfully codoped in the Cu/NCQD skeleton.

Study on fluorescence properties of Cu/NCQDs and NCQDs

To explore the fluorescence performance of the Cu/NCQDs and NCQDs ultraviolet–visible (UV–vis) and fluorescence spectroscopies were performed. Figure 4a and c shows the UV–vis absorption spectra, excitation and emission spectra of the Cu/NCQDs and NCQDs, respectively. Figure 4b and d shows the fluorescence emission spectra of the Cu/NCQDs and NCQDs at different excitation wavelengths, respectively. Notably, the best excitation wavelengths of Cu/NCQDs and NCQDs are 355 nm and 360 nm, respectively. From Fig. 4d, with varying the excitation wavelengths, the maximum emission wavelength of the NCQDs has weak red shift. Notably, with varying the excitation wavelengths, the maximum emission wavelength of the Cu/NCQDs remained 443 nm without any noticeable red or blue shift. This result shows that the water-soluble Cu/NCQDs exhibit PL behavior regardless of the excitation wavelength, which is in contrast to most reported CQDs, whose PL behaviors depend on the excitation wavelength. This PL behavior of the Cu/NCQDs is attributed to its narrow particle-size distribution, as well as its highly uniform surface structure and surface-energy trapping ability (Lin et al. 2018; Bao 2020). Notably, the emission peak of the Cu/NCQDs at 443 nm is independent of the excitation wavelength, this may be related to the proportion of structural defects in CQDs (Fang and Zheng 2021), which reduces the fluorescence interference from the CQDs themselves in the detection process of the target. This evidences the application potential of Cu/NCQDs in the analysis and detection of analytes. By studying the fluorescence performance and QY of Cu/NCQDs and
NCQDs, it can be seen that there is no substantial difference between Cu/NCQDs and NCQDs in fluorescence performance, but Cu/NCQDs have stronger fluorescence intensity, the QY of Cu/NCQDs is considerably improved.

Study of the factors influencing the fluorescence performance of Cu/NCQDs

A series of experiments was conducted to investigate the
Factors affecting the fluorescence performance of the Cu/NCQDs. The experimental results are shown in Fig. 5a. In salt solutions of different concentrations, the fluorescence intensity of the Cu/NCQDs remained almost unchanged, indicating that they are not affected by the solution ionic strength and have excellent salt tolerance. Therefore, Cu/NCQDs can be applied in biochemical analyses. Furthermore, as shown in Fig. 5b, the fluorescence intensity of the Cu/NCQDs is relatively strong and stable in acidic environments. With the increase in the pH, the fluorescence intensity decreases significantly. This phenomenon may be related to the Cu ions on the surface of the Cu/NCQDs, which inhibit hydrolysis in an acidic environment and promote hydrolysis in an alkaline environment. Thus, the content of Cu ions on the quantum dots decreases under alkaline conditions, which decreases the fluorescence intensity. Moreover, several studies have proven the relationship between the fluorescence properties and doped Cu ions (Qing et al. 2020; Han et al. 2021). In addition, the emission wavelength of the Cu/NCQDs does not vary with pH, indicating that the prepared Cu/NCQDs have no dependence on pH. To further measure the photobleaching resistance of the Cu/NCQDs, the same amount of the Cu/NCQD solution was irradiated under a 360 nm UV lamp for 0, 15, 30, 45, 60, 75, 90, 105, and 120 min, after which its fluorescence emission spectrum was measured. As shown in Fig. 5c, with the duration of UV irradiation increased, the fluorescence intensity of the solution barely changed, indicating the excellent photobleaching resistance of the prepared Cu/NCQDs, the stability and persistence of fluorescence were guaranteed, which is essential for their practical application.

**Influence of pH on the determination of metronidazole**

The quenching effect of metronidazole is greatly affected by the detection medium and pH, and the quenching effect of citric acid sodium dihydrogen phosphate buffer solution is the best. Therefore, citric acid sodium dihydrogen phosphate solution was selected as the buffer base to complete the subsequent tests. Considering the strong and stable fluorescent properties of Cu/NCQDs in acidic environment, fixed metronidazole concentration at 100 μmol/L, and citric acid sodium dihydrogen phosphate buffer solutions (2 mol/L) with pH = 2, 3, 4, 5, 6 and 7 were taken, respectively. The fluorescence intensity of 100 μL Cu/NCQDs quenched by metronidazole at the same concentration was investigated. Figure 6 shows the results. When pH = 4, the fluorescence difference ($F_0 - F$) before and after metronidazole quenching was the largest, the quenching effect is the best. Therefore, citric acid sodium dihydrogen phosphate buffer solution with pH = 4 was selected as the base solution for the determination of metronidazole in this experiment.

**Selective detection of metronidazole using Cu/NCQDs**

To evaluate the specificity of this method for metronida- zole detection using Cu/NCQDs, the common potential...
interference substances in metronidazole drugs were studied. The Cu/NCQD solution (100 μL), 2 mL of the citric acid sodium dihydrogen phosphate buffer (pH = 4), and the metronidazole solution (100 μmol/L) were added into a series of 10 mL test tubes. Thereafter, the interference substances (200 mmol/L): K⁺, Mg²⁺, NH₄⁺, Ca²⁺, CO₃²⁻, glucose, ascorbic acid, and sucrose, as well as β-cyclodextrin and L-cysteine (5 mmol/L), were added. The fluorescence intensity was recorded using a fluorescence spectrometer. As shown in Fig. 7, the fluorescence intensities of the solutions with interfering substances (50 and 200 times) and without interfering substances barely changed. The results validated the excellent specificity of the Cu/NCQD fluorescence probe for metronidazole detection.

**Determination of the metronidazole working curve**

Cu/NCQD (100 μL) and metronidazole solutions (100 μL) of different concentrations were added separately to a series of 10 mL test tubes and diluted to scale with the citric acid sodium dihydrogen phosphate buffer (pH = 4). Thereafter, the solution was shaken and left for 5 min; afterward, \( F₀ \) and \( F \) were recorded using the fluorescence spectrometer, and the fluorescence intensity without and with metronidazole was determined using the formula: \( F = F₀ - F \), as shown in Fig. 8. Figure 8a shows the fluorescence spectra of the Cu/NCQD solution with metronidazole in different concentrations, and Fig. 8b shows the corresponding correction curves. The results show that with an increase in the metronidazole concentration in the range of 0–350 μmol/L, the fluorescence intensity of the Cu/NCQDs gradually decreases. The linear equation was \( F = -3.235 + 9.064 C_{(MNZ)}(μmol/L) \), the correlation coefficient \( (R^2) \) was 0.996, and the detection limit was 0.28 μmol/L, calculated by the three times standard deviation method \( (3\sigma/S)(μmol/L) \), \( \sigma \) is the standard deviation of the blank signal \( (n=11) \), and \( S \) is the slope of the linear calibration curve.

**Interaction mechanism between the Cu/NCQDs and metronidazole**

The interaction between the Cu/NCQDs and metronidazole is shown in Fig. 9a. As can be observed, metronidazole exerts a fluorescence quenching effect on the Cu/NCQDs, leading to a decrease in their fluorescence intensity. Therefore, the variation in the fluorescence intensity can be used...
as an indicator of the change in the concentration of metronidazole. Based on this, an on–off fluorescence-detection method using Cu/NCQDs as the fluorescence probe was established for the determination of the metronidazole content. Figure 9a shows that after the addition of metronidazole, the fluorescence emission peak of the Cu/NCQDs did not shift from 443 nm, neither did a new emission peak appear, indicating that the quenching effect of metronidazole on the Cu/NCQDs is independent of the fluorescence resonance energy transfer. To further understand the quenching mechanism of metronidazole on the Cu/NCQD fluorescence, the UV–vis absorption spectrum of metronidazole was compared with the fluorescence excitation spectrum of the Cu/NCQDs (Fig. 9b). In Fig. 9b, metronidazole displays two absorption bands at 230 and 318 nm, whereas the maximum excitation wave peak in the Cu/NCQD spectrum is located at 355 nm. Evidently, the absorption spectrum of metronidazole overlaps with the maximum excitation spectrum of the Cu/NCQDs. Therefore, it can be concluded that the quenching effect of metronidazole on the Cu/NCQD fluorescence is related to the inner filter effect (IFE). In the detection system, metronidazole is the absorber, whereas the Cu/NCQDs are the fluorophore. Metronidazole absorbs the excitation energy of Cu/NCQDs, leading to a decrease in the fluorescence intensity of the Cu/NCQDs. To further determine the quenching mechanism of the system, MNZ and the mixed solution of MNZ and Cu/NCQDs were subjected to UV–vis spectroscopy, as shown in Fig. 9c. After adding the Cu/NCQDs, the characteristic absorption peaks of MNZ did not change, and the electron–hole pair recombination did not occur, indicating that the quenching mechanism was unrelated to the photoinduced electron transfer process. Therefore, in this detection system, the quenching effect of metronidazole on the Cu/NCQDs can be explained by the IFE (Fang and Zheng 2021; Zhao et al. 2018).

Analysis and test of actual samples

The metronidazole-treated tablet solution (20 μL, 11.685 mmol/L) was poured into a 10 mL test tube, and 100 μL of the Cu/NCQD solution was added. Thereafter, the solution was diluted to scale with the citric acid sodium dihydrogen phosphate buffer (pH = 4), and its fluorescence intensity was measured using a fluorescence spectrophotometer. A portion of the honey treatment solution was directly utilized for the fluorescence intensity measurement, and the labeled recovery experiment was conducted simultaneously. The experimental results are listed in Table 1. The calculated MNZ content in the metronidazole tablets was 0.1972 g/tablet, which was not significantly different from the theoretical value (0.2 g/tablet). The recovery rates of the metronidazole tablets and honey samples were 96.8–103.7%, and the relative standard deviation was lower than 6%. The results showed the remarkable application potential of the fluorescence probe in detecting MNZ in actual samples. Compared with other fluorescence-detection methods and the standard methods (Tables 2 and 3, respectively), the results obtained in this paper are close to those of the standard method, which
indicates that the method has reliable application value. Notably, the detection limit of this method is not the lowest, but the linear range is wider. Furthermore, the fluorescent probe of this method uses natural biomass as carbon source and adopts one-step hydrothermal method, which is simpler and more environmentally friendly.

**Conclusion**

Blue fluorescent Cu/NCQDs were successfully synthesized using a simple and green one-step hydrothermal method using frangipani as the carbon source. By introducing Cu and N diheteroatoms, the surface-energy trap of the Cu/NCQDs was effectively passivated using nitrogen-containing groups and Cu-containing groups (N–Cu–N), leading to a non-excitation-dependent fluorescence behavior. Further analysis of Cu/NCQDs showed that the high-fluorescence intensity was stable and long-lasting, and the fluorescence emission was not affected by pH. Therefore, a fluorescence-detection method using Cu/NCQDs as an effective fluorescence probe to determine the metronidazole content in the range of 0–350 μmol/L was established. The $R^2$ value was 0.996, and the detection limit of this method was 0.28 μmol/L. This method was applied to analyze actual samples of medicine tablets and honey, and the results validated its potential for practical application. This method is expected to be advanced into a fluorescence kit for future practical analyses.

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### Table 1

| Samples          | Spiked (μmol/L) | Total found (μmol/L) | Recovery (%) | RSD (%) |
|------------------|-----------------|----------------------|--------------|---------|
| MNZ              | 0               | 23.02 ± 0.21         | –            | –       |
|                  | 20.00           | 42.26 ± 0.24         | 98.2         | 4.3     |
|                  | 40.00           | 65.37 ± 0.46         | 103.7        | 3.6     |
| Commercially available honey | 0               | Not found            | –            | –       |
|                  | 20.00           | 19.35 ± 0.53         | 96.8         | 5.2     |
|                  | 40.00           | 40.43 ± 0.37         | 101.1        | 4.8     |

### Table 2

| Fluorescent probe | Synthetic methods | Carbon source | Linear range (μmol/L) | Detection limit (μmol/L) | Refs. |
|-------------------|-------------------|---------------|-----------------------|--------------------------|-------|
| PCDsa             | Thermal decomposition method | Polyvinyl imine | 0.350–87.6 | 0.12 | Yang (2018) |
| GQDs-embedded SMIPb | _ | Acid magenta6B | 0.2–15 | 0.15 | Kou et al. (2019) |
| g-C3N4 nanosheets | Thermal polymerization | H2O2 | 0.058–0.58 | 0.05 | Hatamiie (2018) |
| CDs               | Solvent hot method | Gardenia | 0.8–225 | 0.28 | Yang et al. (2018) |
| FCNs              | Hydrothermal method | H. cordata | 3.3–240 | 0.12 | Tang et al. (2019) |
| Cu/NCQDs          | Hydrothermal method | Frangipani | 0–350 | 0.28 | Work |

### Table 3

| Methods            | LOD     | Linear range | RSD (%) | Refs.                  |
|--------------------|---------|--------------|---------|------------------------|
| HPLC               | 0.25 μM | 1–200 μM     | < 10    | Zemanová et al. (2022) |
| Electrochemical     | 0.037 μM| 0.1–9.5 μM   | –       | Xia et al. (2021)      |
| Supramolecular fluorescent probe | 65 ng/mL | 0.38–60 μM | 1.4 | Hu (2021) |
| Metal–organic frameworks | 53.4 nM | 1–200 μM | 3 | Zhang et al. (2021) |
| RP–HPLC             | 0.33 μg/mL | 5–15 μg/mL | 2 | Nadendla et al. (2021) |
| HPLC–UV            | 0.08 μg/mL | 0.1–10 μg/mL | < 9.8 | Asma et al. (2022) |
| Cu/NCQDs           | 0.28 μM | 0–350 μM    | < 6     | Work |

This document is a condensed version of the original, focusing on key points and relevant data for clarity and ease of reading.
Declarations

Conflict of interest The authors declare no conflicts of interest.

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