Chalcone-Based Colorimetric Chemosensor for Detecting Ni$^{2+}$

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Abstract: The first chalcone-based colorimetric chemosensor DPP (sodium (E)-2,4-dichloro-6-(3-oxo-3-(pyridine-2-yl)prop-1-en-1-yl)phenolate) was synthesized for detecting Ni$^{2+}$ in near-perfect water. The synthesis of DPP was validated by using $^1$H, $^{13}$C NMR and ESI-MS. DPP selectively sensed Ni$^{2+}$ through the color variation from yellow to purple. Detection limit of DPP for Ni$^{2+}$ was calculated to be 0.36 µM (3σ/slope), which is below the standard (1.2 µM) set by the United States Environmental Protection Agency (EPA). The binding ratio of DPP to Ni$^{2+}$ was determined as a 1:1 by using a Job plot and ESI-mass. The association constant of DPP and Ni$^{2+}$ was calculated as $1.06 \times 10^4$ M$^{-1}$ by the non-linear fitting analysis. In real samples, the sensing application of DPP for Ni$^{2+}$ was successfully performed. DPP-coated paper-supported strips could also be used for detecting Ni$^{2+}$. The binding mechanism of DPP to Ni$^{2+}$ was proposed by ESI-MS, Job plot, UV-vis, FT-IR spectroscopy, and DFT calculations.

Keywords: Ni$^{2+}$; colorimetric sensor; chalcone; test strip; calculations

1. Introduction

Nickel ion is a pivotal metal ion in biological systems, such as respiration, biosynthesis, and metabolism [1]. In addition, it is widely employed in industrial areas, such as Ni-Cd batteries, electropolating, machinery, and catalyst [2–6]. With its industrial usage, a large amount of nickel is released into nature as a pollutant [7], increasing the possibility of nickel exposure. Nickel is toxic, and can cause several illnesses, such as allergies, lung injuries, and respiratory disease [8–11]. Consequently, the acceptable amount of nickel in drinking water recommended by the United States Environmental Protection Agency (EPA) is limited to 1.2 µM [12]. Thus, there is a need to design methods capable of detecting nickel ions easily and quickly in the environment.

Several analytical tools are used to detect Ni$^{2+}$, such as atomic absorption spectrometry, electrochemical methods, inductively coupled plasma mass spectrometry, and fluorescence techniques and distance-based measurement [13,14]. The methods require expensive equipment and a skilled operator [15]. In contrast, the colorimetric chemosensor has no such drawbacks [16–19]. In addition, paper-supported colorimetric sensors adsorbed on paper or thread have an additional benefit, such as semi-quantitative detection with a faster and cheaper analysis [20]. Therefore, it is useful to develop paper-supported colorimetric chemosensors for detecting Ni$^{2+}$. Several colorimetric chemosensors that detect Ni$^{2+}$ were studied in the past few years. Although most of the reported sensors operate in organic solvents, only a few colorimetric chemosensors with functional groups, such as naphthalimide, pyridine, coumarin, Schiff-base, quinone, and polymer with dye detect Ni$^{2+}$ in near-perfect water [21–26]. Thus, the design of colorimetric chemosensors capable of sensing Ni$^{2+}$ in water is of high significance.

Pyridine could provide a binding site for cations [27–29] and have a water-soluble hydrophilic character [30–32]. The chalcone structure has a conjugated $\pi$-electronic system, which provides good chelating ability with metal ions [33–35]. In addition, the $\alpha,\beta$-unsaturated carbonyl in the chalcone structure makes a push–pull chromophore [36,37].
In particular, the chalcone structure can be easily synthesized by using aldol condensation [38]. Thus, we predicted that a chalcone-based chemosensor with a pyridine group can detect metal ions, such as nickel, through a color change in near-perfect water and be applied for paper-supported semi-quantitative detection.

Herein, we present the first chalcone-based colorimetric chemosensor DPP for the detection of Ni\(^{2+}\) in near-perfect water. Chemosensor DPP can sense Ni\(^{2+}\) with a low detection limit by colorimetric variation from yellow to purple. In addition, DPP could apply to real water and its paper-supported strip could detect Ni\(^{2+}\) easily and quickly. The binding mechanism of DPP to Ni\(^{2+}\) was described by UV-visible titrations, ESI-mass, Job plot, FT-IR spectroscopy, and DFT calculations.

2. Materials and Methods

2.1. Materials and Equipment

Sodium hydroxide, 2-acetylpyridine, and 3,5-dichlorosalicylaldehyde were acquired commercially from Alfa, TCI, and Samchun in Korea, respectively. Methanol was acquired from Samchun in Korea. Metal cation solutions were prepared using metal nitrate or perchlorate salts. The pH buffer solutions were acquired commercially from Samchun in Korea. A Varian spectrometer was used to obtain \(^{13}\)C and \(^{1}H\) NMR spectra. Absorption spectra were measured with a Perkin Elmer Lambda 365 UV-Vis. A Thermo MAX instrument was employed to collect ESI-MS spectra. FT-IR spectra were obtained by using a Thermo Fisher Scientific Fourier Transform Infrared Spectrophotometer.

2.2. Synthesis of DPP

DPP was synthesized by the aldol condensation of 2-acetylpyridine and 3,5-dichlorosalicylaldehyde. 2-Acetylpyridine (342 µL, 3.0 mmol) and 10% NaOH 5 mL were added in methanol 15 mL. The solution was stirred for 1 h. Then, 3,5-dichlorosalicylaldehyde (390 mg, 2.0 mmol) was added to the solution, which was additionally stirred at 23 °C for 1 day. The red powder precipitated was filtered, washed with ether, and dried. Yield: 392 mg (61%). \(^{1}H\) NMR: \(\delta = 8.72\) (d, 1H), 8.33 (d, 1H), 8.02 (m, 3H), 7.60 (t, 1H), 7.16 (d, 1H), 7.07 (d, 1H); \(^{13}\)C NMR (175 MHz, DMSO-\(d_{6}\)):\(\delta = 188.87, 167.12, 155.00, 144.42, 137.29, 129.82, 127.32, 126.94, 126.52, 123.18, 121.93, 114.13, 109.01. ESI-mass: \(m/z\) calcd. for C\(_{14}\)H\(_{15}\)Cl\(_2\)NO\(_{2}\)\(-\mathrm{H}_2\)O, 328.02; found, 327.63.

2.3. UV-Vis Titrations

DPP (3.2 mg, 1 \times 10^{-5} mol) was dissolved in DMF (1.0 mL) and 6 µL of the DPP stock (10 mM) was diluted to 2.994 mM PBS buffer (10 mM PBS, pH 7.4) to give 20 mM. Ni(NO\(_{3}\)\(_{2}\) (2.91 mg, 1 \times 10^{-4} mol) was dissolved in 5.0 mL of buffer, and 3-66 µL of the Ni\(^{2+}\) stock (2 \times 10^{-3} M) was added to DPP (2 \times 10^{-5} M). UV-vis spectra were taken after 5 s.

2.4. Job Plot

Then, 3–27 µL of a DPP stock (10 mM) prepared in 1.0 mL of DMF was transferred to several quartzes. Then, 3–27 µL of the Ni\(^{2+}\) solution (1 \times 10^{-2} M) acquired with nitrate salt in a 1.0 mL buffer was added to diluted DPP. Each quartz cell was filled with PBS buffer to 3.0 mL. UV-vis spectra were taken after 5 s.

2.5. Interference Tolerance Test

Sensor DPP (3.2 mg, 1 \times 10^{-5} mol) was dissolved in DMF (1 mL). An amount of 1.0 \times 10^{-4} mol of Al(NO\(_{3}\)\(_{3}\), Cu(NO\(_{3}\)\(_{2}\), Cr(NO\(_{3}\)\(_{3}\)\(_{3}\), Pb(NO\(_{3}\)\(_{2}\), Hg(NO\(_{3}\)\(_{2}\), Co(NO\(_{3}\)\(_{3}\), Ni(NO\(_{3}\)\(_{2}\)\(_{2}\), Ca(NO\(_{3}\)\(_{2}\), Mg(NO\(_{3}\)\(_{2}\), Mn(NO\(_{3}\)\(_{2}\), In(NO\(_{3}\)\(_{3}\), Ga(NO\(_{3}\)\(_{3}\), NaNO\(_{3}\), AgNO\(_{3}\), Fe(NO\(_{3}\)\(_{3}\), Fe(ClO\(_{4}\)\(_{2}\), Cd(NO\(_{3}\)\(_{2}\), and KNO\(_{3}\) was dissolved in 5.0 mL buffer, respectively. An amount of 48 µL of each metal (2 \times 10^{-2} M) and Ni\(^{2+}\) ion (2 \times 10^{-2} M) was added into a 3.0 mL PBS buffer to afford 16 eq., respectively. An amount of 6 µL of the DPP stock (1 \times 10^{-2} M) was added to each solution. A UV-vis spectrum of each solution was taken after 5 s.
2.6. pH Effect

Then, 6 µL of the DPP stock (1 × 10^{-3} M) dissolved in DMF (1.0 mL) was diluted to 2.994 mL of each pH buffer to make 3 × 10^{-5} M. Ni(NO_3)_2 (2.91 mg, 1 × 10^{-4} mol) was dissolved in 5.0 mL buffer solution. Then, 48 µL of the Ni^{2+} stock was added to each DPP. UV-vis spectra were taken after 5 s.

2.7. Water Sample Test by the Spiking Method

The real water sample analysis was performed to determine the spiked Ni^{2+} in samples collected from drinking and tap water in our laboratory. Sensor DPP (3.2 mg, 1 × 10^{-5} mol) was dissolved in DMF (1.0 mL). Then, 6 µL of the DPP stock (1 × 10^{-3} M) was diluted in 2.994 mL of a sample solution containing the spiked Ni^{2+} (6 µM). UV-vis spectra were taken after 5 s.

2.8. Test Strip

The test strip assay was achieved with DPP. Filter paper cut into pieces was dipped in a DPP media at a concentration of 1 mM (1.0 mL, MeOH) and dried for 1 h. After the filter paper completely dried off, various concentrations (10, 50, and 100 µM) of Ni^{2+} solutions dissolved in buffer were employed to determine the lowest visible amount. A concentration of 50 µM of varied cation solutions (Zn^{2+}, Al^{3+}, Mn^{2+}, K^+, Cd^{2+}, Fe^{2+}, Ca^{2+}, Fe^{3+}, Cr^{3+}, Hg^{2+}, Mg^{2+}, Cu^{2+}, Co^{2+}, Pb^{2+}, In^{3+}, Na^+, Ga^{3+}, and Ni^{2+}) was employed to analyze the selectivity of the test strip.

2.9. Calculations

The detecting mechanism of DPP to Ni^{2+} was investigated by using the Gaussian16 program [39] for theoretical calculations. They were based on B3LYP density functional methods [40,41]. The 6-31G(d,p) [42,43] and Lanl2DZ [44] basis sets were used for calculations of elements and Ni^{2+}, respectively. The solvent effect of water was checked by employing IEFPCM [45]. With the optimized patterns of DPP and DPP-Ni^{2+}, 20 of the lowest triplet-triplet transitions were calculated by using the TD-DFT method to investigate the transition states of the two compounds.

3. Results and Discussion

DPP was gained by the aldol condensation of 2-acetylpyridine and 3,5-dichlorosalicylaldehyde and affirmed by ^1H NMR, ^13C NMR, and ESI-mass (Figure 1).

![Figure 1. Cont.](image-url)
Figure 1. Cont.
Figure 1. (a) Synthesis scheme of DPP. (b) $^1$H NMR spectrum of DPP. (c) $^{13}$C NMR spectrum of DPP. (d) Negative-ion mass spectrum of DPP (100 µM).

3.1. Spectroscopic Studies of DPP with Ni$^{2+}$

Colorimetric sensing capability of DPP was examined with cations (Zn$^{2+}$, Al$^{3+}$, Mn$^{2+}$, K$^+$, Cd$^{2+}$, Fe$^{2+}$, Ca$^{2+}$, Fe$^{3+}$, Cr$^{3+}$, Hg$^+$, Mg$^{2+}$, Cu$^{2+}$, Co$^{2+}$, Pb$^{2+}$, In$^{3+}$, Na$^+$, Ga$^{3+}$, and Ni$^{2+}$) in buffer (pH = 7.4, Figure 2).

Figure 2. Cont.
In adding diverse cations to DPP, only Ni$^{2+}$ showed significant spectral change with a prominent increase of 550 nm (Figure 2a) and distinguishable color change from yellow to purple (Figure 2b). Meanwhile, other cations did not exhibit any significant spectral or visual changes, suggesting that DPP can sense exclusively Ni$^{2+}$ with a color change. We executed the UV-vis titration to analyze the binding feature of DPP with Ni$^{2+}$. As the Ni$^{2+}$ was added into DPP, the absorbance of 373 nm and 550 nm was prominently increased, and that of 325 nm and 453 nm was visibly decreased. A complete isosbestic point was detected at 391 nm, suggesting that sensor DPP and Ni$^{2+}$ would create a species (Figure 2c). In particular, DPP is the first chalcone-based sensor among chemosensors previously addressed for the sensing of Ni$^{2+}$ in near-perfect water (Table 1).

**Table 1.** Examples of chemosensors for detection of Ni$^{2+}$.

| Sensor | Detection Limit (μM) | Test Strip | Reference |
|--------|----------------------|------------|-----------|
| ![Sensor](image) | 0.057 | Yes | [21] |
| ![Sensor](image) | 0.074 | No | [22] |
| ![Sensor](image) | 0.037 | No | [23] |

Figure 2. (a) Absorption variations of DPP (20 μM) with cations (20 eq.). (b) Color variations of DPP (20 μM) with different cations (20 eq.). (c) Absorption variations of DPP (20 μM) with varied amounts of Ni$^{2+}$ (0–16 eq.).
A Job plot experiment was achieved to determine the binding feature of DPP and Ni^{2+} (Figure 3). The result illustrated that DPP and Ni^{2+} made a 1:1 binding stoichiometry.

Figure 3. Job plot for DPP with Ni^{2+} at 550 nm.

The 1:1 stoichiometry was assured by the ESI-MS test (Figure 4). The peak of 385.73 (m/z) was assignable to be [(DPP + Ni^{2+} − Na^{+} + 2H_{2}O)]^{+} [calcd. 385.95].

According to the calibration curve with nickel ion, the association constant of DPP and Ni^{2+} was calculated as $1.06 \times 10^{4}$ M$^{-1}$ by the non-linear fitting analysis (Figure 5a) [46]. Detection limit of DPP to Ni^{2+} was determined as 0.36 μM (3σ/slope, Figure 5b).

| Sensor | Detection Limit (μM) | Test Strip | Reference |
|--------|----------------------|------------|-----------|
| ![Structure 1](image1.png) | 0.0012 | No | [24] |
| ![Structure 2](image2.png) | - | No | [25] |
| ![Structure 3](image3.png) | 1.78 | No | [26] |
| ![Structure 4](image4.png) | 0.36 | This work | |

Table 1. Cont.
Figure 4. Positive-ion mass spectrum of DPP ($1 \times 10^{-5}$ M) with Ni(NO$_3$)$_2$ (1.0 eq.).

Figure 5. (a) Association constant based on variation in the ratio (absorbance at 550 nm) of DPP (20 µM) with Ni$^{2+}$. The Redline is the nonlinear fitting obtained, assuming a 1:1 binding of DPP and Ni$^{2+}$. (b) Analysis of the detection limit for Ni$^{2+}$ by DPP (20 µM). The standard deviations are represented by the error bar ($n = 3$).
Furthermore, FT-IR analysis was performed to investigate the interaction of DPP and Ni\(^{2+}\) (Figure 6). The band at 1644 cm\(^{-1}\) associated with the carbonyl group (C=O) of DPP moved to 1619 cm\(^{-1}\) [47,48], signifying that the carbonyl oxygen might bind to Ni\(^{2+}\).

![FT-IR spectra of (a) DPP and (b) DPP-Ni\(^{2+}\).](image)

**Figure 6.** FT–IR spectra of (a) DPP and (b) DPP-Ni\(^{2+}\).

With the outcomes of Job plot, ESI-mass, and IR analysis, the possible feature of DPP with Ni\(^{2+}\) was proposed (Scheme 1).

![Proposed feature of DPP-Ni\(^{2+}\).](image)

**Scheme 1.** Proposed feature of DPP-Ni\(^{2+}\).
The inhibition experiment was conducted to identify the exclusive selectivity of DPP for Ni\(^{2+}\) in a competitive environment (Figure 7).

![Figure 7](image_url)

**Figure 7.** (a) Absorption variations of DPP (20 µM) with Ni\(^{2+}\) (20 eq.) and metal ions (20 eq.). (b) Color variations of DPP (20 µM) with Ni\(^{2+}\) (20 eq.) and metal ions (20 eq.).

When nickel and other metals of the same concentration existed together, DPP was hardly disturbed by other metals except for Cr\(^{3+}\). The detecting ability of DPP to Ni\(^{2+}\) was inspected in a pH range of 6–9 (Figure 8).

![Figure 8](image_url)

**Figure 8.** Cont.
DPP showed the ability to sense Ni\(^{2+}\) at pH 7–9. Test-strip experiments were performed with filter papers coated with DPP for practical application. DPP showed a colorimetric change from yellow to purple at 50 \(\mu\)M Ni\(^{2+}\) (Figure 9a) and selectively detected Ni\(^{2+}\) among varied metal ions (Figure 9b). This result indicated that DPP could be applied to detecting Ni\(^{2+}\) by using a test strip.

The real water sample analysis was performed to determine the spiked Ni\(^{2+}\) in samples collected from drinking and tap water (Table 2).

**Table 2. Determination of Ni\(^{2+}\).**

| Sample    | Ni\(^{2+}\) Added (µM) | Ni\(^{2+}\) Found (µM) | Recovery (%) | R.S.D (n = 3) (%) |
|-----------|------------------------|-------------------------|--------------|------------------|
| Drinking water | 0.0                    | 0.0                     | -            | -                |
| Tap water   | 0.0                    | 5.98                    | 99.68        | 0.24             |

\(^a\) Conditions: [DPP] = 20 \(\mu\)M in PBS buffer.
The acceptable recovery percentage and relative standard deviation (R.S.D.) were obtained, meaning that DPP could measure Ni$^{2+}$ substantially in a real environment.

3.2. Theoretical Study

To understand the sensing process of DPP to Ni$^{2+}$, theoretical calculations of DPP and DPP-Ni$^{2+}$ were carried out. The calculations of DPP-Ni$^{2+}$ were based on the 1:1 association of DPP and Ni$^{2+}$, which was suggested by ESI-MS and Job plot. The energy-optimized structures of DPP and DPP-Ni$^{2+}$ are shown in Figure 10.

The dihedral angle (6N, 1C, 11C, and 12O) of DPP is calculated as 27.06°, showing a twisted structure. DPP-Ni$^{2+}$ complex with the dihedral angle of −3.84° forms a tetrahedral structure with 2H$_2$O. With the energy-optimized structures, TD-DFT calculations were performed to study the electron transitions of DPP and DPP-Ni$^{2+}$. For DPP, excited state 1 (472.73 nm) was regarded to be the HOMO → LUMO transition, which showed an ICT character (Figures 11 and 12). Its molecular orbitals indicated the shift of electron cloud from the 2,4-dichlorophenol moiety to the pyridine one. The ICT character contributes to the yellow color of DPP. For DPP-Ni$^{2+}$, excited state 8 (553.47 nm) consists of the HOMO → LUMO (alpha), HOMO → LUMO+1 (beta), and HOMO → LUMO+2 (beta). The HOMO → LUMO (alpha) showed the ICT character from the 2,4-dichlorophenol group to the pyridine one. The HOMO → LUMO+1 (beta) and HOMO → LUMO+2 (beta) displayed both the ICT characters from the 2,4-dichlorophenol group to the pyridine one and LMCT characters from DPP to nickel (Figures 12 and 13).

In addition, the calculated excitation energy of DPP-Ni$^{2+}$ decreased compared to free DPP when the complex was formed (Figure 12). Calculated theoretical values demonstrated the redshift of the UV-vis transitions, which is consistent with experimental results. With Job plot, ESI-MS, DFT calculations, and FT-IR, we proposed the colorimetric sensing of Ni$^{2+}$ by DPP (Scheme 1).
Figure 11. (a) The experimental UV-vis and theoretical excitation energies of DPP. (b) The significant electronic transition energies and MO contributions for DPP (H = HOMO and L = LUMO).

| Excited state 1 | Wavelength (nm) | Percent (%) | Main Character | Oscillator strength |
|-----------------|-----------------|-------------|---------------|---------------------|
| H → L           | 472.73          | 99%         | ICT           | 0.4149              |

Figure 12. MO diagrams and excitation energies of DPP and DPP-Ni$^{2+}$. 
Figure 13. (a) The experimental UV-vis and theoretical excitation energies of DPP-Ni$^{2+}$. (b) The significant electronic transition energies and MO contributions for DPP-Ni$^{2+}$ (H = HOMO and L = LUMO).

4. Conclusions

We developed a chalcone-based colorimetric chemosensor DPP that can efficiently detect Ni$^{2+}$ by a colorimetric variation from yellow to purple. With Job plot and ESI-MS, the association mode of DPP to Ni$^{2+}$ was analyzed to be a 1:1 ratio. The detection limit and binding constant of DPP to Ni$^{2+}$ were 0.36 µM and 1.06 × 10$^4$ M$^{-1}$, respectively. The detection limit of DPP is below the United States Environmental Protection Agency (EPA) guideline (1.2 µM) for Ni$^{2+}$. It is noteworthy that DPP is the first chalcone-based colorimetric chemosensor to detect Ni$^{2+}$ in near-perfect aqueous media. Practically, DPP could recognize Ni$^{2+}$ in real water. In addition, the DPP-coated paper-supported strip showed a clear color variation from yellow to purple only in Ni$^{2+}$. The binding mechanism of DPP to Ni$^{2+}$ was explained by Job plot, ESI-mass, UV-vis, FT-IR, and calculations.

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