2,7-Naphthyridine based colorimetric and fluorescent “Turn Off” chemosensors for selective detection of Ni(II) in aqueous media

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Abstract

A highly selective and sensitive 2,7-naphthyridine based colorimetric, reversible, pH independent and fluorescence “Turn Off” chemosensors (**L1-L4**) for detection of Ni^{2+} are being reported in aqueous media. The synthesized sensors are highly efficient in detecting Ni^{2+} even in the presence of other metal ions that commonly co-exist with nickel. The receptors (**L1-L4**) showed a distinct color change from yellow to red by addition of Ni^{2+} with spectral changes in bands at 535–550 nm. The detection limit of Ni^{2+} for (**L1-L4**) are in the range of 0.2–0.5 μM which is 2–5 times lower than the permissible value of Ni^{2+} (1.2 μM) in drinking water defined by EPA. The binding mode of interactions of **L1-L4** for Ni^{2+} were found to be 2:1 through job's plot and ESI-MS analysis. Moreover the receptors can be used to quantify Ni^{2+} in real water samples and formation of test strips by dip-stick method increases the practical applicability of Ni^{2+} test for “in-the-field” measurement of Ni^{2+} . Importantly the sensing potential of these derivatives have been tuned by the nature of substituents i.e. electron donating (CH_3) and electron attracting (F , OCF_3), which showed that **L4** is highly efficient in sensing of Ni^{2+} even at minute level.

Introduction

The development and synthesis of chemosensors for selective and sensitive detection of heavy and transition metal ions is an active area of present day research due to their substantial effects on environment and biological systems ^{1–3}. The sensing of metal ions in aqueous media is provocative task due to presence of competitive interactions between the solvent and guest for receptor binding sites ^{4,5}. Among the various transition metals, nickel is an important element due to its wide spread use in industry (Ni-Cd batteries), in ceramics and magnetic types of computers, metallurgical processes (electroplating), rods for arc welding, surgical and dental prostheses, pigments for paints ^{6–8}. Nickel has significant role in various enzymatic activities such as acireductone dioxygenases, carbon monoxide dehydrogenases, and catalyst for hydrogenation. It is also used as essential trace element in biological systems which has significance in biosynthesis and metabolism of some plants and microorganisms. However it is toxic metal in bio-medicine point of view as it can be easily absorbed in our different organs like spleen liver, kidney etc that might cause lungs cancer and nasopharyngeal carcinoma, asthma, disorder of respiratory as well as central nervous system in humans, pneumonitis. The deficiency and excessive use of nickel also affects the life of many prokaryotic and eukaryotic organisms ^{9–13}.

Considering all these facts, the selective monitoring of nickel is very important in environmental, biological and industrial samples. Although various analytical methods such as flame atomic absorption spectrometry-electro thermal atomization (FAS-ETA), atomic absorption spectrometry (AAS), inductively coupled plasma atomic emission spectrometry (ICP-AES) are widely used for detection of metal ions ^{14–19}. However, most of the methods need trained operators, sophisticated equipment and tedious sample preparation procedures therefore there is still a need of simple, efficient and cost-effective methods for the micro level detection of heavy metals ions. Now a days, colorimetric, ratiometric, potentiometric and

fluorescence sensors have gained the attention for selective detection of metal ions (Ni^{2+}) in biological and environmental samples. Colorimetric chemosensors showed a distinct visible color change without the use of expensive equipment. Therefore colorimetric sensors seem to be more promising due to low cost, rapid detection and simple-to-use than classical techniques and fluorescent sensors as well. Only a few number of colorimetric chemosensors for the detection of Ni^{2+} at parts per million level are reported to date²⁰.

Benzo[*c*]pyrazolo[2, 7]naphthyridines and its derivatives have gained prodigious attention in last few decades because they are biologically active alkaloids isolated from marine organisms such as perlolidine²¹ (cellulose inhibitor), subarine²² (anti-HIV activity), meridine²³ (cytotoxic activity), amphimedine^{24,25} (top isomerase II) inhibitor) and PDK-1 inhibitors²⁶.

Thus in perpetuation of our research work for the development in the field of molecular recognition, we herein report benzo[*c*]pyrazolo[2, 7] naphthyridine-5,6-diamine based efficient colorimetric and/or *fluorescent off* sensors that can detect Ni^{2+} with sensitivity and selectivity in aqueous solutions. According to literature, structural motifs of amino group containing sensors like diaminonaphthalene **1**²⁷, 1,8-naphthyridine-amine **2**²⁸, 1,8-naphthyridine-2-acetoamide **3**²⁹, diaminophenazine **4** and 1,2-diaminoanthracene-dione **5**³⁰, are being known to sense different metal ions like Cu^{2+} , Hg^{2+} , Fe^{3+} , Al^{3+} etc.

To the best of our knowledge, this is the first report in which benzo[*c*]pyrazolo[2, 7]naphthyridines have been explored as chromophore and two amino groups as binding sites for the selective detection of Ni^{2+} in aqueous solutions. Moreover the novel synthesized chemosensors **L1-L4** could be used as practical sensor for quantitative determination of nickel at ppm level in real water samples. Importantly the sensing potential of these derivatives can be tuned by the nature of substituents i.e. electron donating (CH_3) and electron attracting (F , OCF_3), which affect the metal ions sensing property.

Results And Discussion

The benzo[*c*]pyrazolo[2,7]naphthyridine based chemosensors were synthesized as shown in **scheme 1**. The isatin **6** react with malononitrile **7** via Knoevenogel condensation to form arylidene. The formed arylidene then reacted with 3-amino-5-methylpyrazole **8** to synthesize the spiro-intermediates which then undergo basic hydrolysis, cyclization, decarboxylation and aromatization to form target naphthyridine receptors (**L1-L4**)³¹.

The Ni^{2+} complex of receptor **L4** was synthesized by mixing Ni^{2+} salt with **L4** using 1:2 ratio in DMSO- H_2O solvent mixture. The yellow solution of the ligand immediately turned to red colored solution. The solution was further refluxed to get the solid product (**Scheme 2**).

Spectrophotometric studies of L1–L4

The chemosensor study of **L1–L4** towards various metal ions (Al^{3+} , Ca^{2+} , Cd^{2+} , Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{3+} , Hg^{2+} , K^{+} , Mg^{2+} , Mn^{2+} , Na^{+} , Ni^{2+} , Pb^{2+} , Sr^{2+} and Sn^{2+}) were investigated by UV-visible spectroscopy. The preliminary colorimetric experiments revealed that addition of one equivalent of metal ions (1×10^{-3} M) to solution of **L1–L4** (1×10^{-3} M) in DMSO– H_2O (v/v 1:2), HEPES buffer of pH = 7.4 at room temperature resulted in distinct visual color change from yellow to red by addition of Ni^{2+} and no color change was observed for other metal ions (Al^{3+} , Ca^{2+} , Cd^{2+} , Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{3+} , Hg^{2+} , K^{+} , Mg^{2+} , Mn^{2+} , Na^{+} , Pb^{2+} , Sr^{2+} and Sn^{2+}) **Figure 2**.

The binding interaction of **L1–L4** with different metal ions was further monitored by investigating UV-visible absorption spectral changes and shown in **Table 1**.

Table 1: UV-visible spectral bands of receptor **L1-L4** with addition of nickel (II).

Receptor	UV-visible spectral band (nm)	Nickel addition
L1	273, 283, 398, 440	535 nm
L2	274, 286, 384, 443	538 nm
L3	261, 287, 380, 450	550 nm
L4	273, 285, 396, 438	537 nm

The UV-visible spectra of model receptor **L4** showed a remarkable bathochromic shift in absorption spectrum at 537 nm which is in good agreement with color change, may possibly be ascribed to fast metal-ligand binding kinetics and high thermodynamic affinity of Ni^{2+} for N-donor ligands³². The other examined metal ions did not exhibit any distinct spectral changes in UV-visible spectrum at 537 nm under identical conditions. Similar pattern of absorption spectral changes were observed for **L1-L3** (**Figure S1-S3**).

The coordination between receptor **L4** and Ni^{2+} was further ratified by UV-visible absorption spectral titrations involving sequential addition of Ni^{2+} (0-12 μM) to **L4** (20 μM). It was observed that intensity of absorption bands at 537 nm and 438 nm increased while the absorption bands at 396 nm and 376 nm began to decrease until it reached its limiting value. Moreover emergence of isosbestic points at 365 nm and 410 nm during spectral titrations indicate the formation of stable complex with some stoichiometric ratios between **L4** and Ni^{2+} ³³ (**Figure 3**). The similar coordination behavior was observed for **L1-L3** (**Figure S4-S6**). These results suggest that receptors **L1-L4** could be employed as colorimetric and ratiometric sensor for Ni^{2+} and discriminating among different transition metal ions (Fe^{3+} , Cu^{2+} , Co^{2+} , Pb^{2+} , Hg^{2+}) which are normally difficult to differentiate.

The binding stoichiometry of the complexes were further explored by Job’s continuous variation method³⁴ by plotting mole fraction versus changes in absorption intensity at 535 nm for **L1**, 538 nm for **L2**, 550 nm for **L3** and 537 nm for **L4**, respectively. The Job’s plot (**Figure S7**) indicate maximum value at 0.7 corresponding to the formation of complex with 2:1 stoichiometry between **L1–L4** and metal ions Ni^{2+} .

The association constant K_a of receptors **L1–L4** with Ni^{2+} were determined by Benesi–Hildebrand equation ³⁵ (**Figure S8**) and are listed in **table 2**. It has been clear that the association constant values are in range of those 10^3 - 10^6 reported for Ni^{2+} sensing chemosensors ³⁶. The comparison of K_a values shows that **L4- Ni²⁺** complex is stronger than the other receptor complexes.

Table 2: Association constant values and detection limit of receptor **L1-L4** with nickel (II).

Receptor	Association constant M ⁻¹	Detection limit (3S _B /S) M	Detection limit (Naked eye) M
L1	2.3 x 10 ³	5.62 x 10 ⁻⁷	1 x 10 ⁻⁵
L2	1.0 x 10 ⁴	5.56 x 10 ⁻⁷	1 x 10 ⁻⁵
L3	2.6 x 10 ⁴	3.88 x 10 ⁻⁷	1 x 10 ⁻⁵
L4	3.2 x 10 ⁴	2.43 x 10 ⁻⁷	1 x 10 ⁻⁶

The detection limit of **L1–L4** for Ni^{2+} as colorimetric sensors were determined both by naked eye and absorption spectral changes. The results are shown in **Table 2**. For naked eye detection, the receptor **L4** showed a distinct color change at minimum concentration of 1 x 10⁻⁶ M for Ni^{2+} (**Figure 4/S9**). Moreover, the detection limit determined by absorption spectral changes on the basis of 3S_B/S ³⁷ for **L4** and Ni^{2+} was found to be 2.43 x 10⁻⁷ M. This value is five times lower than EPA drinking water guidelines 1.2 x 10⁻⁶ M for Ni^{2+} ³⁸ and revealed that **L4** is highly efficient in sensing Ni^{2+} even at minute level.

The possible binding mode of receptor **L4** and Ni^{2+} in the complex showed that the nitrogen atoms of naphthyridines coordinates Ni^{2+} in 2:1 ratio and showed bathochromic shift in absorption spectra that can be rationalized by ICT ³². The coordination of Ni^{2+} to the nitrogen of naphthyridine moiety increases its electron withdrawing character which showed stronger ICT from electron donating methyl group to metal complex moiety.

ESI-MS and IR titrations

The coordination mechanism of **L4** was further explored by ESI-MS and IR titration experiments. The ESI mass spectra of **L4** showed the appearance of peak at m/z 279.17 corresponds to **[L4+ H]⁺**. The titration of **L4** with Ni^{2+} showed the signal at m/z 685.58 for **[2L4+Ni+Cl₂]⁺** ions indicating the formation of 2:1 stoichiometry between **L4** and Ni^{2+} (**Figure S10**).

FT-IR titrations were performed by using Bruker Alpha FT-IR and **Figure 5** showed comparison of IR spectra of **L4** before and after the addition of Ni^{2+} . The sharp peaks present at 3420, 3294 and 3109 cm⁻¹

due to NH stretching frequencies in free receptor **L4** were broadened by adding Ni^{2+} , suggesting the involvement of NH_2 group in coordination with Ni^{2+} to form complex.³⁹

Metal ion selectivity

An important feature of receptor **L4** is to examine its selectivity towards analyte by competitive titration experiments (**Figure 6**). The intensity of absorption band at 537 nm due to complex formation of **L4**- Ni^{2+} is not disturbed at all in the presence of other metal ions (Al^{3+} , Ca^{2+} , Cd^{2+} , Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{3+} , Hg^{2+} , K^+ , Mg^{2+} , Mn^{2+} , Na^+ , Pb^{2+} , Sr^{2+} and Sn^{2+}). Thus receptor **L4** shows excellent binding affinity for Ni^{2+} in other physiological samples where Cu^{2+} , Co^{2+} , Fe^{3+} , Hg^{2+} and Pb^{2+} usually coexist with analyte. This distinct selectivity for Ni^{2+} may be due to suitable conformation of receptor and ionic radius of Ni^{2+} ¹³.

The UV-visible absorption spectra of **L4**- Ni^{2+} complex with various anions was recorded to check the stability of complex, no change in absorption band at 537 nm was observed (**Figure 7**). This clearly depicts that the stability of complex is unaffected in the presence of various anions.

pH effect study

In order to investigate the effect of pH on absorption response of receptor **L4** to Ni^{2+} , a series of solution with pH value ranging from (2.0 – 12.0) were prepared (**Figure S11**).

At pH 2.0–3.0, the receptor **L4** has no substantial response to Ni^{2+} in absorption spectroscopy. The absorption at 537 nm is maximum and constant in pH range 7.0 – 8.0 and above pH 8.0, absorbance decreased gradually. The results warranted its biological and environmental applications at physiological pH. The color of **L4**- Ni^{2+} complex remained red between pH 4–11, which indicates that Ni^{2+} could be clearly detected over a wide range of pH 4–11.

Reversibility of receptor L4

The reversibility of receptor **L4** towards Ni^{2+} was examined by adding ethylenediaminetetraacetic acid (EDTA, 1 equiv.) to the complexed solution of **L4** and Ni^{2+} (**Figure 8**). The solution color changed from red to light yellow (original color of **L4**). Upon addition of Ni^{2+} again the absorbance at 537 nm was recorded. The absorption changes in spectral bands were reversible even after several cycles with alternative sequential addition of Ni^{2+} and EDTA. These results indicate that receptor **L4** could be recyclable through reagent EDTA. Such regeneration and reversibility could be valuable for the fabrication of sensors to sense Ni^{2+} .

Fluorescence study

The fluorescence study of **L4** via fluorescence titrations were examined at room temperature and exhibited emission maximum at 470 nm ($\lambda_{\text{ex}} = 390\text{nm}$). The sequential addition of Ni^{2+} (0 – 12 μM) to the receptor **L4** caused a reasonable decrease of emission intensity in emission maxima at 470 nm and

gave bounteous information regarding “*turn-off*” behavior of receptor (**Figure 9**). The quenching of fluorescence (CHEQ) may be due to coordination of Ni^{2+} with NH_2 group of receptor **L4** as amine group loses its donating ability to fluorophore and emission potential is quenched ⁴⁰.

Chemistry synthesized of L4– Ni^{2+} complex

The synthesized complex of L4– Ni^{2+} was characterized in terms of molar conductance, SEM and ESMIS analysis. The 10^{-3} M solution of L4– Ni^{2+} complex exhibited molar conductance value of $0.4 \text{ S cm}^2 \text{ M}^{-1}$ which suggest its non-electrolyte behavior in DMSO solution. Furthermore, SEM analysis was carried out to get better understanding of morphological difference before and after the addition of Ni^{2+} to **L4** receptor (**Figure 10**). SEM images of receptor **L4** has dense sprinkled elliptical shape like structure which has been transformed into rough stone like structure after complexation with Ni^{2+} . The ESI-MS of synthesized L4– Ni^{2+} complex (**Figure S12**) showed the molecular ion peak at m/z 685.58 which resembled very well with experimental molar mass of $[2\text{L4}+\text{Ni}+\text{Cl}_2]$ complex.

Practical application

In order to investigate the potential use of newly synthesized receptor **L4** in real water samples, a calibration curve was drawn, which showed good linear relationship ($R^2 = 0.9996$, $n = 3$) between the absorbance of L4– Ni^{2+} complex and Ni^{2+} concentration (0–5 μM) at 537 nm (**Figure 14/S11**).

The receptor **L4** was used for estimation of Ni^{2+} in drinking water, tap water and industrial waste water samples (**Table 3**). All water samples were analyzed in triplicate with good recoveries and RSD values. The results indicate that receptor **L4** is highly specific and sensitive for Ni^{2+} estimation in environmental samples.

Table 3: Determination of Ni^{2+} in water samples

Sample	Ni^{2+} added (μM)	Ni^{2+} found (μM)	Recovery (%)	RSD (n = 3) %
Drinking water	0.00	0.00	98.0	1.97
	1.00 ^a	0.98 ^b		
		1.00 ^c		
Tap water	0.00	0.00	97.0	2.34
	1.00 ^a	0.97 ^b		
		1.00 ^c		
Industrial waste water	0.00	0.00	96.0	3.04
	1.00 ^a	0.96 ^b		
		0.99 ^c		

^a = 1.00 μM of Ni^{2+} was spiked artificially.

^b = Results obtained by newly synthesized receptor **L4**.

^c = Results obtained from ICP-OES.

To explore another application of receptor **L4**, test kits were prepared by immersing filter paper in receptor **L4** (1×10^{-3} M, HEPES buffer, pH = 7.4) and then air dried to check the suitability of “dip-stick” method for detection of Ni^{2+} . When the prepared test strips were immersed into water solution of Ni^{2+} with different concentrations, clear color change from yellow to red was observed (**Figure 11**). The results showed that discernible concentration of Ni^{2+} can be as low as 1×10^{-5} M. The development of “dip-stick” method did not require any additional equipment for detection of Ni^{2+} and showed extreme attraction “in-the-field” measurements.

Conclusion

In summary, we have successfully characterized the photophysical properties of benzo[d]pyrazolo[2,7]naphthyridines (**L1-L4**) for the first time which were prepared by green synthetic route. The receptor (**L1-L4**) promotes selective and sensitive sensing of Ni^{2+} in aqueous media over a wide range of pH (4–11) even in the presence of competitive ions i.e Fe^{3+} , Cu^{2+} , Co^{2+} . A unique colorimetric response to Ni^{2+} is observed (yellow to red) through coordination of receptor and Ni^{2+} complex could be recyclable through treatment with EDTA. The detection limit of Ni^{2+} were found to be in range of 0.2–0.5 μM for (**L1-L4**) which is 2–5 times lower than the permissible value of Ni^{2+} (1.2 μM) in drinking water defined by American Environmental Protection Agency (EPA). The binding mode of interactions of (**L1-L4**) for Ni^{2+} were found to be 2:1 through job's plot and ESI-MS analysis. The fluorescence properties of receptor were evaluated with fluorescence quenching by coordination with Ni^{2+} . As a practical application, the most efficient receptor **L4** could be used to quantify and detect Ni^{2+} in real water samples and also applied for fabrication to test kit by using “dip-stick” method. The result indicate that to the best of our knowledge, receptor (**L1-L4**) are the first reported multifunctional, naked eye chemosensors for sensing of Ni^{2+} in aqueous solutions.

Experimental

Materials and equipment

All the solvents and reagents used for synthesis were of analytical grade and used as received. Infrared (IR) spectra were recorded by Bruker Alpha FT-IR spectrophotometer. Mass spectra were recorded by Thermo Scientific LTQ-XL system fitted with electrospray ionization (ESI) source, Jeol 600 MS Route, and Jeol Hx110 mass spectrometer (EI-HR). Pre-coated aluminum sheets of silica gel 60 GF254 (Merck) were used as TLC plates to check the purity of compounds. Quantitative determination of nickel was carried out by Inductively Coupled Plasma-Optical Emission Spectrometer (iCAP6500 ICP-OES, Thermo Scientific, Cambridge, United Kingdom). The pH was measured by using Metrohm, 781 pH/ion meter.

Synthesis of receptors (**L1-L4**)

The synthesis of receptors (**L1–L4**) was carried out in two steps following our previously reported protocol³¹

Synthesis of **L4-Ni²⁺** complex

The DMSO (3 ml) solution of **L4** (0.2 mmol) and 2 ml water solution of NiCl₂·6H₂O (0.12 mmol) were mixed and stirred at room temperature for 30 min. The yellow solution of receptor **L4** was immediately turned to red colored solid product. It was filtered and washed with distilled water.

Red solid, Yield: 84%, mp > 300 °C; IR (ATR, cm⁻¹): 3368, 3222, (NH), 1642, 1541, 1438, 1339, 1238, 1110, 1031, 1002, 825, 731; MS (ESI) m/z: 685.41 [2L4+Ni+Cl₂]⁺; Molar conductance: 0.41 S cm² M⁻¹.

UV-visible and fluorescence titrations

Stock solutions of receptors, **L1–L4** (1×10⁻³ M) were prepared in DMSO–H₂O (v/v = 1:2) using HEPES buffer solution (pH = 7.4). Stock solutions of different guest metal ions (1×10⁻³ M) were prepared by using chloride salts of the respective metals (Al³⁺, Ca²⁺, Cd²⁺, Co²⁺, Cr³⁺, Cu²⁺, Fe³⁺, Hg²⁺, K⁺, Mg²⁺, Mn²⁺, Na⁺, Ni²⁺, Pb²⁺, Sr²⁺ and Sn²⁺) and the stock solutions (1×10⁻⁴ M) of different anions like Cl⁻, I⁻, Br⁻, CN⁻, ClO₄⁻, F⁻, HSO₄⁻, AcO⁻ and SCN⁻ from TBA salts were prepared in deionized water. For ratiometric titrations, the solutions of various concentrations of receptor with increasing concentration of cations were prepared separately.

Competition experiments

For Ni²⁺ the stock solution of receptor **L4** (1×10⁻³ M) was prepared in DMSO–H₂O (v/v 1:2) using HEPES buffer of pH = 7.4. Stock solution of different guest cations (1×10⁻³ M) were prepared in water and added to 4 mL of the solution of receptor **L4** to give 10 equivalent of metal ions. Then Ni²⁺ solution was added into mixed solution of each metal ion to make 1 equivalent. After few minutes of mixing them, the UV-visible spectra was recorded at room temperature.

Water sample collection and Ni²⁺determination

The drinking water samples, tap water and industrial waste water samples were collected, preserved and stored in plastic containers for Ni²⁺ analysis. Industrial waste water samples were filtered prior to analysis. Each sample was analyzed in triplicate using receptor **L4** and ICP-OES as standard method (**Table 3**). Spiking and recovery method was used in order to validate chemosensing performance of our newly developed sensor **L4**. UV–visible spectral measurement of water samples containing Ni²⁺ was carried out by adding 0.5 mL of receptor **L4** to 2.5 mL of sample solutions and pH of solution was maintained at 7.4 using HEPES buffer. The solutions were allowed to stand for 10 min at room temperature and absorption measurements were taken at 537 nm. Filtered water samples were directly used for ICP-OES analysis.

Colorimetric test strips

The test kits were prepared by immersing filter paper strips in to receptor **L4** solution 1×10^{-3} M (DMSO–H₂O (v/v 1:2) using HEPES buffer of pH = 7.4) and then dried in air. Then the pure water solution with different Ni²⁺ concentrations were prepared and the prepared test strips were immersed in water samples and color change from yellow to red was observed.

References

1. Mulrooney, S. B. & Hausinger, R. P. Nickel uptake and utilization by microorganisms. *FEMS microbiology reviews*. **27**, 239–261 (2003).
2. Ragsdale, S. W. Nickel-based enzyme systems. *Journal of Biological Chemistry*. **284**, 18571–18575 (2009).
3. Maier, R. (Portland Press Ltd., 2005).
4. Singh, A., Singh, A. & Singh, N. A Cu (II) complex of an imidazolium-based ionic liquid: synthesis, X-ray structure and application in the selective electrochemical sensing of guanine. *Dalton Trans.* **43**, 16283–16288 (2014).
5. Raj, P. *et al.* Fluorescent chemosensors for selective and sensitive detection of phosmet/chlorpyrifos with octahedral Ni²⁺ complexes. *Inorg. Chem.* **55**, 4874–4883 (2016).
6. Ragsdale, S. W. Nickel and Its Surprising Impact in Nature. Metal Ions in Life Sciences, Vol. 2. Edited by Astrid Sigel, Helmut Sigel, and Roland K. 140. Sigel(2008).
7. Kasprzak, K. S., Sunderman Jr, F. W. & Salnikow, K. Nickel carcinogenesis. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*. **533**, 67–97 (2003).
8. Kuck, P. Nickel. United States Geological Survey, Mineral Commodity Summaries, January 2006. *United States Geological Survey*, 116–117(2006).
9. Zambelli, B., Musiani, F., Benini, S. & Ciurli, S. Chemistry of Ni²⁺ in urease: sensing, trafficking, and catalysis. *Accounts of chemical research*. **44**, 520–530 (2011).
10. Staton, I. *et al.* Dermal nickel exposure associated with coin handling and in various occupational settings: assessment using a newly developed finger immersion method. *British Journal of Dermatology*. **154**, 658–664 (2006).
11. Stangl, G. I., Eidelsburger, U. & Kirchgessner, M. Nickel deficiency alters nickel flux in rat everted intestinal sacs. *Biological trace element research*. **61**, 253 (1998).
12. Heim, K. E. & McKean, B. A. Children's clothing fasteners as a potential source of exposure to releasable nickel ions. *Contact dermatitis*. **60**, 100–105 (2009).
13. Prabhu, J. *et al.* A simple chalcone based ratiometric chemosensor for sensitive and selective detection of Nickel ion and its imaging in live cells. *Sensors and Actuators B: Chemical*. **238**, 306–317 (2017).

14. Ohta, K., Ishida, K., Itoh, S., Kaneco, S. & Mizuno, T. Determination of nickel in water by electrothermal atomic absorption spectrometry with preconcentration on a tungsten foil. *Microchim. Acta*. **129**, 127–132 (1998).
15. Sarre, S., Van Belle, K., Smolders, I., Krieken, G. & Michotte, Y. The use of microdialysis for the determination of plasma protein binding of drugs. *Journal of pharmaceutical and biomedical analysis*. **10**, 735–739 (1992).
16. Mazloum, M., Niassary, M. S. & Amini, M. K. Pentacyclooctaaza as a neutral carrier in coated-wire ion-selective electrode for nickel (II). *Sensors and Actuators B: Chemical*. **82**, 259–264 (2002).
17. Jankowski, K., Yao, J., Kasiura, K., Jackowska, A. & Sieradzka, A. Multielement determination of heavy metals in water samples by continuous powder introduction microwave-induced plasma atomic emission spectrometry after preconcentration on activated carbon. *Spectrochimica Acta Part B: Atomic Spectroscopy*. **60**, 369–375 (2005).
18. Zendelovska, D., Pavlovska, G., Cundeva, K. & Stafilov, T. Electrothermal atomic absorption spectrometric determination of cobalt, copper, lead and nickel traces in aragonite following flotation and extraction separation. *Talanta*. **54**, 139–146 (2001).
19. Sunil, A. & Rao, S. J. First derivative spectrophotometric determination of copper (II) and nickel (II) simultaneously using 1-(2-hydroxyphenyl) thiourea. *Journal of Analytical Chemistry*. **70**, 154–158 (2015).
20. Biswas, S., Acharyya, S., Sarkar, D., Gharami, S. & Mondal, T. K. Novel pyridyl based azo-derivative for the selective and colorimetric detection of nickel (II). *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. **159**, 157–162 (2016).
21. Reissert, A. Ueber Di-(γ -amidopropyl) essigsäure (Diamino. 1.7. heptanmethylsäure. 4) und ihr inneres Condensationsproduct, das Octohydro. 1.8. naphthyridin. *Berichte der deutschen chemischen Gesellschaft*. **26**, 2137–2144 (1893).
22. Bobrański, B. & Sucharda, E. Über eine Synthese des 1.5-Naphthyridins. *Berichte der deutschen chemischen Gesellschaft (A and B Series)*. **60**, 1081–1084 (1927).
23. Schmitz, F. J., DeGuzman, F. S., Hossain, M. B. & Van der Helm, D. Cytotoxic aromatic alkaloids from the ascidian *Amphicarpa meridiana* and *Leptoclinides* sp.: Meridine and 11-hydroxyascididemin. *The Journal of Organic Chemistry*. **56**, 804–808 (1991).
24. Tejeria, A. *et al.* Antileishmanial effect of new indeno-1, 5-naphthyridines, selective inhibitors of *Leishmania infantum* type IB DNA topoisomerase. *European Journal of Medicinal Chemistry*. **124**, 740–749 (2016).
25. Schmitz, F. J., Agarwal, S. K., Gunasekera, S. P., Schmidt, P. G. & Shoolery, J. N. Amphimedine, new aromatic alkaloid from a pacific sponge, *Amphimedon* sp. Carbon connectivity determination from natural abundance carbon-13-carbon-13 coupling constants. *Journal of the American Chemical Society*. **105**, 4835–4836 (1983).
26. Goutham, K., Kadiyala, V., Sridhar, B. & Karunakar, G. V. Gold-catalyzed intramolecular cyclization/condensation sequence: synthesis of 1, 2-dihydro [c][2, 7] naphthyridines. *Org. Biomol.*

- Chem.* **15**, 7813–7818 (2017).
27. Qu, L., Yin, C., Huo, F., Zhang, Y. & Li, Y. A commercially available fluorescence chemosensor for copper ion and its application in bioimaging. *Sensors and Actuators B: Chemical*. **183**, 636–640 (2013).
28. Zhu, Y. *et al.* A reversible fluorescent chemosensor for the rapid detection of mercury ions (II) in water with high sensitivity and selectivity. *RSC Adv.* **4**, 61320–61323 (2014).
29. Yao, D., Huang, X., Guo, F. & Xie, P. A new fluorescent enhancement chemosensor for Al³⁺ and Fe³⁺ based on naphthyridine and benzothiazole groups. *Sensors and Actuators B: Chemical*. **256**, 276–281 (2018).
30. Udhayakumari, D., Velmathi, S., Sung, Y. M. & Wu, S. P. Highly fluorescent probe for copper (II) ion based on commercially available compounds and live cell imaging. *Sensors and Actuators B: Chemical*. **198**, 285–293 (2014).
31. Ashraf, A. *et al.* one-pot, multi-component, green synthesis of substituted benzo [c] pyrazolo [2, 7] naphthyridines. *RSC Advances*. **10**, 5938–5950 (2020).
32. Jiang, J., Gou, C., Luo, J., Yi, C. & Liu, X. A novel highly selective colorimetric sensor for Ni (II) ion using coumarin derivatives. *Inorg. Chem. Commun.* **15**, 12–15 (2012).
33. Goswami, S. *et al.* A highly selective ratiometric chemosensor for Ni²⁺ in a quinoxaline matrix. *New Journal of Chemistry*. **38**, 6230–6235 (2014).
34. Job, P. Job's method of continuous variation. *Ann. chim* **9** (1928).
35. Benesi, H. A. & Hildebrand, J. A spectrophotometric investigation of the interaction of iodine with aromatic hydrocarbons. *Journal of the American Chemical Society*. **71**, 2703–2707 (1949).
36. Kang, J. H., Lee, S. Y., Ahn, H. M. & Kim, C. A novel colorimetric chemosensor for the sequential detection of Ni²⁺ and CN[−] in aqueous solution. *Sensors and Actuators B: Chemical*. **242**, 25–34 (2017).
37. Committee, A. M. Recommendations for the definition, estimation and use of the detection limit. *Analyst*. **112**, 199–204 (1987).
38. Dhanushkodi, M. *et al.* A simple pyrazine based ratiometric fluorescent sensor for Ni²⁺ ion detection. *Dyes and Pigments*. **173**, 107897 <https://doi.org/10.1016/j.dyepig.2019.107897> (2020).
39. Liu, Y. L. *et al.* A New Fluorescent Chemosensor for Cobalt (II) Ions in Living Cells Based on 1, 8-Naphthalimide. *molecules* **24**, 3093 (2019).
40. Son, Y. A., Gwon, S. Y. & Kim, S. H. A Colorimetric and Fluorescent Chemosensor for Ni²⁺ Based on Donor- π -Acceptor Charge Transfer Dye Containing 2-Cyanomethylene-3-Cyano-4, 5, 5-Trimethyl-2, 5-Dihydrofuran Acceptor and 4-Bis (pyridin-2-ylmethyl) Aminobenzene Donor. *Journal of nanoscience and nanotechnology*. **12**, 1503–1506 (2012).

Schemes

Schemes 1 and 2 can be found in the Supplemental Files section.

Figures

Figure 1

Some structural motifs of amino group containing sensors and present study.

Figure 2

(a) Absorption spectral changes of L4 (20 μM) in the presence of different metal ions in DMSO–H₂O (v/v 1:2, HEPES buffer pH = 7.4). (b) Visual colorimetric response of receptor L4 upon addition of one equivalent various metal ions.

Figure 3

Absorbance titration spectra of receptor L4 (20 μM) in the presence of various concentrations of Ni^{2+} (0–12 μM) in DMSO–H₂O (v/v 1:2, HEPES buffer, pH = 7.4)

Figure 4

Naked eye detection limit for receptor L4.

Figure 5

IR spectra of (a) receptor L4 and (b) receptor L4–Ni²⁺ complex.

Figure 6

Absorbance responses of L4 (20 μM) in the presence of Ni²⁺ (10 μM) with 10 equivalents of various metal ions in DMSO–H₂O (v/v = 1:2) HEPES buffer solutions at pH = 7.4.

Figure 7

(a) Absorbance at 537 nm of receptor L4 (20 μ M) in the presence of Ni^{2+} (10 μ M) in the presence of 10 equivalents of various anions in DMSO–H₂O (v/v = 1:2) HEPES buffer solutions at pH = 7.4. b) The color changes of L4 upon addition of Ni^{2+} and various anions (1-10).

Figure 8

(a) Absorbance at 537 nm of receptor L4 (20 μM) in the presence of Ni^{2+} (10 μM) in the presence of 10 equivalents of various anions in DMSO–H₂O (v/v = 1:2) HEPES buffer solutions at pH = 7.4. b) The color changes of L4 upon addition of Ni^{2+} and various anions (1–10).

Figure 9

(a) Fluorescence spectra of receptor L4 (20 μM) in the presence of various concentrations of Ni^{2+} (0–12 μM) HEPES buffer, pH = 7.4 (λ_{ex} = 390 nm) (b) Proposed detection mechanism of receptor L4 to Ni^{2+} .

Figure 10

The SEM images of a) Receptor L4 b) L4- Ni²⁺ complex

Figure 11

Color change of the test strips of L4 (1×10^{-3} M) at various concentrations of Ni²⁺ in water, from left to right: 0, 1×10^{-3} M, 1×10^{-4} M, 1×10^{-5} M and 1×10^{-6} M.

Supplementary Files

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