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RESEARCH ARTICLE

Fe³⁺-SELECTIVE “OFF-ON” PROBE BASED ON NAPHTHALIMIDE MODIFIED BENZOYL HYDRAZINE DERIVATIVELin Li¹, Yulin Zhou¹, Wanting Dai¹, Chunwei Yu^{1*}, Siyu Huang¹ and Jun Zhang^{1,2*}¹Laboratory of Environmental Monitoring, School of Tropical and Laboratory Medicine, Hainan Medical University, Haikou, 571199, China;²Laboratory of Tropical Biomedicine and Biotechnology, Hainan Medical University, Haikou 571101, China

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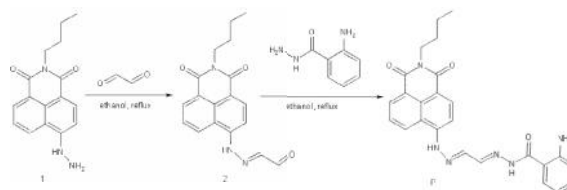
ABSTRACT

A new “off-on” probe for Fe³⁺ based naphthalimide modified benzoyl hydrazine derivative was designed and synthesized. The proposed probe P showed good selectivity to Fe³⁺ compared to other common metal ions and anions. The absorbance of P was proportional to the concentration of Fe³⁺ in the range of 9.0 × 10⁻⁶ to 6.5 × 10⁻⁵ M with a detection limit of 3.0 × 10⁻⁶ M.

Keywords:Probe, Fe³⁺, Naphthalimide, Benzoyl Hydrazine.

INTRODUCTION

The essential role of Fe³⁺ ion in human and animal health became apparent with identification of Fe³⁺ ion as a body constituent and realization of the relationship between adequate intake and prevention of certain diseases (M. N. Elizabeth, *et al*, 2008). However, deficiencies or excesses of this ion are toxic or can lead to a variety of diseases, such as Parkinson's disease and Alzheimer's disease (Y. S. Jeong, *et al*, 2012). Therefore, detection of this biologically important and cytotoxic ion in physiological milieu and animal cells has important consequences in biological and environmental concerns. Even though considerable efforts have been undertaken to develop fluorescent probes for Fe³⁺, Fe³⁺ amplified photophysical properties with high selectivity over other interfering heavy metal ions are extremely scarce due to its inherent paramagnetic nature (L. C. Li, *et al*, 2018; C. W. Yu, *et al*, 2018; M. Kumar, *et al*, 2018; J. H. Hu, *et al*, 2017; D. Shi, *et al*, 2015). So far the signal transduction occurrence via chelation enhanced response with these inherent quenching metal ions may be desirable for analytical purposes to construct “off-on” probes in biological and environmental sample (M. H. Lee, *et al*, 2010; M. Y. She, *et al*, 2012; W. T. Yin, *et al*, 2011; Z. Yang, *et al*, 2012; N. R. Chereddy, *et al*, 2012; J. D. Charters, *et al*, 2011). In this work, a new compound derived from benzoyl hydrazine was characterized as Fe³⁺-selective probe (Scheme 1).



Scheme 1. Synthesis route of probe P

Experimental Section

Reagents and Instruments: All reagents and solvents are of analytical grade and used without further purification. UV-Vis spectra were obtained on a Hitachi U-2910 spectrophotometric. Mass (MS) spectra were recorded on a Thermo TSQ Quantum Access Agilent 1100 system. Nuclear magnetic resonance (NMR) spectra were measured with a Bruker AV 400 instrument and chemical shifts are given in ppm from tetramethylsilane (TMS).

Synthesis of Compound**Synthesis of Compound 3**

Compound 1 was synthesized according to the reported method (C. W. Yu, *et al*, 2014). Under N₂ gas, compound 1 (2.9 mmol) was stirred in ethanol (40 mL), glyoxal (4.4 mmol) in ethanol (10 mL) was added dropwise. The reaction mixture was stirred at 80 °C for 6 h, and then cooled to room temperature. The yellow precipitate so obtained was filtered and dried under vacuum and used directly. Yields: 60.8%.

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Synthesis of Compound P: Under N_2 gas, compound 2 (0.16 mmol) and 2-aminobenzohydrazide (0.15 mmol) were combined in ethanol (40 mL) and stirred. The mixture was then heated under reflux for 5 h and monitored by TLC. After the reaction was completed, the solution was cooled to room temperature. The precipitate so obtained was filtered and washed with cold ethanol. The crude product was purified by recrystallization from ethanol to afford P. Yields: 75.8%. 1H NMR: 11.79 (s, 1H), 11.65 (s, 1H), 8.50 (d, 1H), 8.38 (s, 1H), 8.20 (d, 1H), 8.29 (d, 1H), 7.83 (d, 1H), 7.63 (s, 2H), 7.55 (d, 1H), 7.23 (d, 1H), 6.76 (d, 1H), 6.61 (t, 1H), 6.59 (b, 2H), 4.03 (t, 2H), 1.59 (d, 2H), 1.34 (d, 2H), 0.92 (t, 3H).

General Spectroscopic Methods: Metal ions and probe P were dissolved in deionized water and DMSO to obtain 1.0 mM stock solutions, respectively. Before spectroscopic measurements, the solution was freshly prepared by diluting the high concentration stock solution to the corresponding desired concentration.

RESULTS AND DISCUSSION

Selectivity of P toward metal ions and anions: To evaluate the selectivity of probe P, the UV spectra of P (10 μ M) were investigated in ethanol with the addition of respective metal ions (100 μ M) (Figure 1). Tested ions and anions are K^+ , Na^+ , Ca^{2+} , Mg^{2+} , Zn^{2+} , Pb^{2+} , Co^{2+} , Cd^{2+} , Cu^{2+} , Fe^{2+} , Cr^{3+} , Ni^{2+} , Hg^{2+} , Cu^+ , Fe^{3+} , Al^{3+} , Ag^+ , ClO_4^- , NO_3^- , CO_3^{2-} , ClO_4^- , Br^- , SO_4^{2-} , I^- and HPO_4^{2-} . Study showed that compared to other ions examined, only Fe^{3+} generated a significant UV response of the monomeric peak at 350 nm with absorbance enhancement. These results suggested that P had a higher selectivity toward Fe^{3+} than the other metal ions and anions. Furthermore, in the competition experiment, the UV properties of P toward other metal ions and anions (above-mentioned) were also measured (Figure 2). The increase of absorbance resulting from the addition of the Fe^{3+} was not influenced by the addition of excess metal ions and anions. All of these indicated that P was a highly selective and sensitive colorimetric P for Fe^{3+} in ethanol.

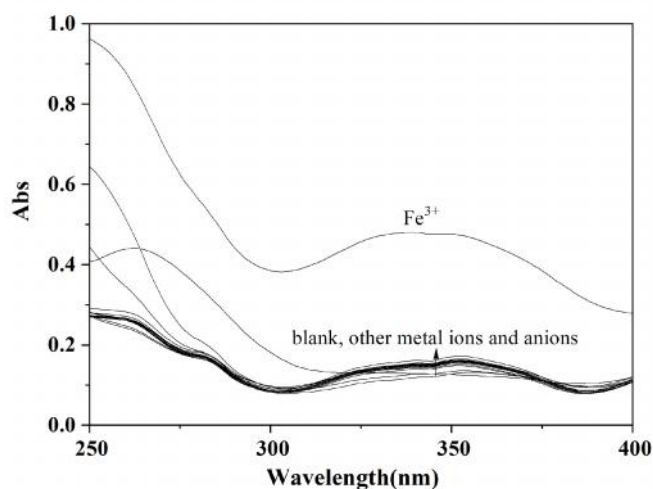


Figure 1. Absorption spectra of P (10 μ M) to different metal ions and anions (100 μ M) in ethanol

UV Spectral Response of P toward Fe^{3+} : To further investigate the interaction of Fe^{3+} and P, an UV titration experiment was carried out. The result showed that the absorbance of P was enhanced regularly upon addition of various amounts of Fe^{3+} in

ethanol as depicted in Figure 3. Under the present conditions, when P was employed at 10 μ M level, the absorbance of P was proportional to the concentration of Fe^{3+} in the range of 9.0×10^{-6} to 6.5×10^{-5} M with a detection limit of 3.0×10^{-6} M. This clearly demonstrated that probe P could sensitively detect environmentally relevant levels of Fe^{3+} . These results clearly suggested the binding of P with Fe^{3+} .

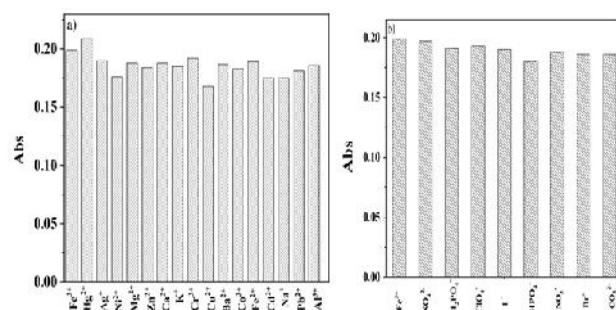


Figure 2 a) UV response of P (10 μ M) to Fe^{3+} (10 μ M) and to the mixture of different metal ions (10 μ M) with Fe^{3+} (10 μ M); b) UV response of P (10 μ M) to Fe^{3+} (10 μ M) and to the mixture of different individual anions (10 μ M) with Fe^{3+} (10 μ M) in ethanol.

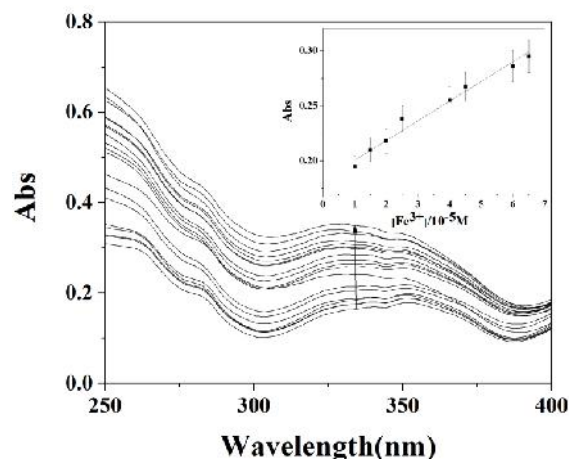


Figure 3. UV response of P (10 μ M) to various concentrations of Fe^{3+} in ethanol. Inset: the absorption spectra at 350 nm of P (10 μ M) as a function of Fe^{3+} concentrations (0–6.5 μ M)

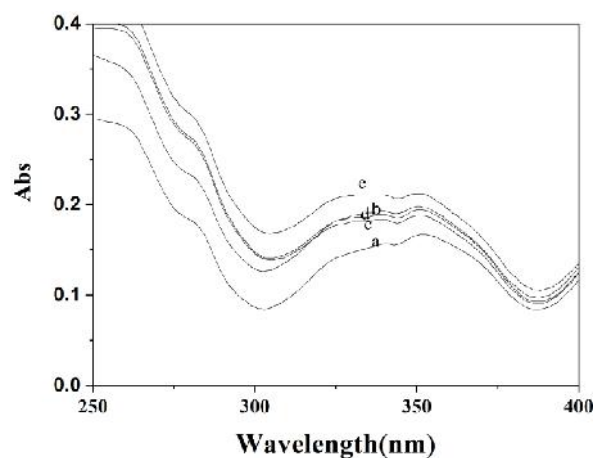


Figure 4 The absorption spectra in ethanol: (a) P (10 μ M); (b) P (10 μ M) with Fe^{3+} (10 μ M); (c) P (10 μ M) with Fe^{3+} (10 μ M) and then addition of EDTA (10 μ M); (d) P (10 μ M) with Fe^{3+} (10 μ M) and then addition of EDTA (10 μ M) and then addition of 0.1 mM Fe^{3+}

Reversibility of P toward Fe³⁺: It is believed that this process is not reversible, which has been proved by the test using EDTA-Fe³⁺ as seen in Figure 4, without Fe³⁺, P existed in a unconstrained C=N form (Figure 4a), addition of Fe³⁺ led to coordination with the ligand groups, resulting in a constrained C=N form along with an obvious increase absorbance at 350 nm (Figure 4b), which is not influenced obviously by addition of EDTA. Thus, the most likely binding sites for Fe³⁺ are the conjugated moieties including atoms. It is very likely due to the chelation-induced constrained C=N form. Thus, an “off-on” based probe for Fe³⁺ was constructed.

Conclusions

In conclusion, we have developed a new probe for Fe³⁺ to induce enhanced absorbance change. The probe was selective and sensitive for Fe³⁺, capable of detecting the metal ion low to 3 μM. Further studies include the design of new analogues of P with good solubility in water which enable the practical application of these types of Fe³⁺ probes will to be implemented. This work was financially supported by the Research and Training Foundation of Hainan Medical University (No. HY2019-11810123) and the National Natural Science Foundation of China (No. 81860381, 81760387).

REFERENCES

- Chartres J.D., Busby M., Riley M.J., Davis J.J., Bernhardt P.V. 2011. A turn-on fluorescent iron complex and its cellular uptake. *Inorg Chem.*, 50: 9178-9183.
- Cherreddy N.R., Suman K., Korrapait P.S., Thennarasu S., Mandal A.B. 2012. Design and synthesis of rhodamine based chemosensors for the detection of Fe³⁺ ions. *Dyes Pigm.*, 95: 606-613.
- Elizabeth M.N., Stephen J.L. 2008. Tools and tactics for the optical detection of mercuric ion. *Chem.Rev.*, 108: 3443-3480.
- Hu J.H., Li J.B., Sun Y., Pei P.X., Qi J. 2017. A turn-on fluorescent chemosensor based on acylhydrazone for sensing of Mg²⁺ with a low detection limit. *RSC Adv.*, 7: 29697-29701.
- Jeong Y.S., Yoon J.Y. 2012. Recent progress on fluorescent chemosensors for metal ions. *Inorg Chim Acta.*, 381: 2-14.
- Kumar M., Kumar A., Faizi M.S.H., Kumar S., Singh M.K., Sahu S.K., Kishor S., John R.P. 2018. A selective ‘turn-on’ fluorescent chemosensor for detection of Al³⁺ in aqueous medium: Experimental and theoretical studies. *Sens. Actuators B: Chem.*, 260: 888-899.
- Lee M.H., Giap T.V., Kim S.H., Lee Y.H., Kang C.H., Kim J.S. 2010. A novel strategy to selectively detect Fe(III) in aqueous media driven by hydrolysis of a rhodamine 6G Schiff base. *Chem Commun.*, 46: 1407-1409.
- Li L.C., Guan R.F., Guo M.M., Ning P., Shao R., Meng X.M. 2018. A FRET based two-photon fluorescent probe for ratiometric detection of Pd²⁺ in living cells and *in vivo*. *Sens. Actuators B: Chem.*, 254: 949-955.
- She M.Y., Yang Z., Yin B., Zhang J., Gu J., Yin W.T., Li J.L., Zhao G.F., Shi Z. 2012. A novel rhodamine-based fluorescent and colorimetric “off-on” chemosensor and investigation of the recognizing behavior towards Fe³⁺. *Dyes Pigm.*, 92: 1337-1343.
- Shi D., Yang F.Y., Wang M., Zou Y., Zheng T.C., Zhou X.G., Chen L. 2015. Rhodamine derivative functionalized chitosan as efficient sensor and adsorbent for mercury(II) detection and removal. *Mater. Res. Bull.*, 70: 958-964.
- Yang Z., She M.Y., Yin B., Cui J.H., Zhang Y.Z., Sun W., Li J.L., Shi Z. 2012. Three rhodamine-based “off-on” chemosensors with high selectivity and sensitivity for Fe³⁺ imaging in living cells. *J. Org. Chem.*, 77: 1143-1147.
- Yin W.T., Cui H., Yang Z., Li C., She M.Y., Yin B., Li J.L., Zhao G.F., Shi Z. 2011. Facile synthesis and characterization of rhodamine-based colorimetric and “off-on” fluorescent chemosensor for Fe³⁺. *Sens. Actuators B: Chem.*, 157: 675-680.
- Yu C.W., Jian L., Ji Y.X., Zhang J. 2018. Al(III)-responsive “off-on” chemosensor based on rhodamine derivative and its application in cell imaging. *RSC Adv.*, 8: 31106-31112.
- Yu C.W., Wen Y.Y., Qin X., Zhang J. 2014. A fluorescent ratiometric Cu²⁺ probe based on FRET by naphthalimide-appended rhodamine derivatives. *Anal. Methods.*, 6: 9825-9830.
