

A Highly Fluorescent Pyrene-based Sensor for Selective Detection of Fe³⁺ Ion in Aqueous Medium: DFT and Molecular Docking Studies

Puthiyavalappil Rasin

National Institute of Technology Tiruchirappalli

Merlin Mary Mathew

National Institute of Technology Tiruchirappalli

Vipin Manakkadan

National Institute of Technology Tiruchirappalli

Vishnunarayanan Namboothiri Vadakkedathu Palakkeezhillam

National Institute of Technology Tiruchirappalli

Sreekanth Anandaram (✉ sreekanth@nitt.edu)

National Institute of Technology Tiruchirappalli <https://orcid.org/0000-0002-2942-8487>

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Abstract

In this work, we introduce a highly selective and sensitive fluorescent sensor based on pyrene derivative for Fe(III) ion sensing in DMSO/water media. 2-(pyrene-2-yl)-1-(pyrene-2-ylmethyl)-1H-benzo[d]imidazole (PEBD) receptor was synthesized via simple condensation reaction and confirmed by spectroscopic techniques. The receptor exhibits fluorescence quenching in the presence of Fe(III) ions at 440 nm. ESI-MS and Job's method were used to confirm the 1:1 molar binding ratio of the receptor PEBD to Fe(III) ions. Using the Benesi-Hildebrand equation the binding constant value was determined as $8.485 \times 10^3 \text{ M}^{-1}$. Furthermore, the limit of detection (LOD, $3\sigma/K$) value was found to be $1.81 \mu\text{M}$ in DMSO/water (95/5, v/v) media. According to the Environmental Protection Agency (EPA) of the United States, it is lower than the acceptable value of Fe^{3+} in drinking water (0.3 mg/L). The presence of 14 other metal ions such Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{2+} , Hg^{2+} , Pb^{2+} , K^+ , Ni^{2+} , Mg^{2+} , Cd^{2+} , Ca^{2+} , Mn^{2+} , Al^{3+} , and Zn^{2+} did not interfere with the detection of Fe(III) ions. Computational studies of the receptor PEBD were carried out with density functional theory (DFT) using B3LYP/ 6-311G (d, p), LANL2DZ level of theory. Finally, molecular docking studies have been performed to investigate the Cytochrome P450 1A1(CYP1A1) protein inhibitory action of the receptor PEBD.

Introduction

In the last few years, the amount of different metal ions in the diet has been increased due to environmental pollution and many other natural activities [1]. The level of metal ions beyond the desirable limit can cause different chronic diseases in humans including cancer, Parkinson's disease, and Alzheimer's diseases [2-5]. So the design and development of facile, sensitive, and selective metal ion sensors are very important since many of the sensors provide naked-eye detection of different metal ions. Iron plays a major role in various biological activities in human beings such as transmitting nerve signals, regulating water content and osmotic pressure, muscle contraction, proton transfer, and enzyme synthesis [6-9]. The intake of iron either from daily food or through supplements is crucial in maintaining different mechanisms and metabolic activities in the human body. Iron deficiency can further cause anemia which leads to abnormal heartbeats and even organ damages[10]. Despite its biological importance, a high concentration of iron in the human body leads to unbalanced body functions and can trigger many side effects. Iron toxicity can prevent oxidative phosphorylation and mitochondrial function [11]. Iron can be accumulated in the human body if its intake is very high, and which eventually leads to brain or liver damage [12]. Also, previous reports revealed that the concentration of iron above 3 ppm in drinking water can alter its colour and taste [13]. Apart from this, it has been observed that a significant level of iron in water can enhance the growth of different bacteria including *Toxothrix trichogenes*, *Leptothrix orchracea*, and *Gallionella feruginea* [14]. Also, the development of these bacteria in water pipelines can cause biofilms, deposition of ferric hydroxide, and corrosion in metal pipelines [15].

In this context, the design and development of different sensors for the detection of iron are very important for controlling its concentration in different foods, water, and biological systems. Based on the

chemical properties of iron different techniques have been used for its identification both qualitatively and quantitatively. Among these techniques, atomic absorption spectroscopy (AAS) is a precise method used for the determination of iron concentration in water [16]. Several restrictions are associated with AAS and other sophisticated instruments when compare with chemical sensors [17]. Chemical sensors are easy to design and the cost of manufacture is comparatively very low. Also, their selectivity and sensitivity can be easily varied by modifying them according to the target [18]. Whereas highly sophisticated instruments are costly and require experts to handle them. The bulkiness of the instrument and the need for ambient conditions for its storage and working restricted their use in laboratory conditions. So an effective and easily accessible sensor is required for the detection of iron in different samples. For this purpose, fluorescence sensors are highly recommendable. In This study, we introduce the synthesis of a pyrene-based fluorescent sensor for the detection of Fe(III) in essentially pure water. It can be highlighted that this sensor can specifically detect Fe (III) ion over the presence of other cations such as Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{2+} , Hg^{2+} , Pb^{2+} , K^+ , Ni^{2+} , Mg^{2+} , Cd^{2+} , Ca^{2+} , Mn^{2+} , Al^{3+} , and Zn^{2+} . The sensor has been synthesized in a single step by the condensation of 1-pyrenecarboxaldehyde with benzene-1,2-diamine in the presence of glacial acetic acid as a catalyst. Also, molecular docking studies have been performed to understand the interactions between the sensor and Cytochrome P450 1A1(CYP1A1) protein.

Materials And Methods

Chemicals and instruments

All chemicals used in the study were of AR grade and used as received. Chloride salts of various metal ions (Fe^{3+} , Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{2+} , Hg^{2+} , Pb^{2+} , K^+ , Ni^{2+} , Mg^{2+} , Cd^{2+} , Ca^{2+} , Mn^{2+} , Al^{3+} , and Zn^{2+}) were used to examine the sensing behavior of the compound PEBD. Millipore water was collected from the Millipore water purification system (Thermo Scientific Barnstead Smart2Pure Pro UV/UF 16 LPH). The characterization of the receptor PEBD and the complex PEBD- Fe^{3+} were done with several spectroscopic methods. The ^1H NMR and the ^{13}C NMR spectra were recorded on a Bruker, 500 MHz in DMF at 298 K with TMS as an internal standard. A Perkin-Elmer F1-IR/ FIR spectrometer in the range of $400\text{-}4000\text{ cm}^{-1}$ was used to record the FT-IR spectra of the compounds. UV-Visible spectra were recorded on an Analytical Jena specords 600 UV-Vis diode-array spectrophotometer. Similarly, emission spectra were measured using a Jasco V-630 Spectrofluorometer. Mass spectra of the receptor PEBD and the complex PEBD- Fe^{3+} were obtained on an Agilent mass spectrometer.

Synthesis of the receptor PEBD

The pyrene based sensor ([[(N1E,N2E)-N1,N2-bis(pyrene-1-ylmethylene)benzene-1,2-diamine]] (PEBD) was developed and purified by adopting and modifying a reported procedure [19]. The compound was obtained at a high yield. The procedure is given in the supplementary document file.

Fluorescent studies of the receptor PEBD

A stock solution of the receptor PEBD (1×10^{-3} M) was prepared in DMSO by dissolving 2.66 mg in 5 mL and diluted to a concentration of 1×10^{-5} M. Investigated the fluorescent behavior of the receptor PEBD system (1×10^{-5} M) in DMSO/water (95/5, v/v) and the emission wavelength was found to be 440 nm. The chloride salts of different metals are used in the sensing studies. 1×10^{-3} M aqueous solution of all the metal salts are prepared in Millipore water. The excitation wavelength of the receptor PEBD was 280 nm.

For a better understanding of the sensing properties of receptor PEBD towards Fe^{3+} , fluorescent titration experiments were performed at 440 nm. The limit of detection (LOD) value of the receptor PEBD was obtained from the equation $3\sigma/K$ (where σ is the standard deviation of the blank solution and K represents the slope of the calibration curve between fluorescent intensity and the Fe^{3+} concentrations). The selectivity and interference studies of the receptor PEBD towards Fe^{3+} were carried out by excitation at 280 nm in presence of different metal ions.

Theoretical DFT calculations

To predict the electronic behavior and properties of the individual atoms, computational studies of the compounds PEBD and PEBD- Fe^{3+} were carried out with density functional theory (DFT) using B3LYP/ 6-311G (d, p), LANL2DZ level of theory. Furthermore, frontier molecular orbital analysis (FMO) and molecular electrostatic potential map (MEP) were also carried out for predicting the chemical reactivity and the energy levels (HOMO and LUMO) of the receptor PEBD and PEBD- Fe^{3+} complex.

Molecular docking studies

Molecular docking is a useful tool generally used to design drug molecules that identify the preferred binding sites of proteins and nucleic acids, which predicts the presence of various noncovalent interactions [20]. In the present study, molecular docking studies have been performed to investigate the biological activities of the receptor PEBD using Auto Dock vina. The structure of protein cytochrome P450 1A1 (CYP1A1) was retrieved from the protein data bank (PDB ID: 418V). All the docked possess were visualized using Discover Studio and Pymol software.

Results And Discussion

Synthesis and characterization of the receptor (PEBD)

The compound ($[(\text{N1E}, \text{N2E})\text{-N1}, \text{N2}\text{-bis}(\text{pyrene-1-ylmethylene}) \text{benzene-1,2-diamine}]$) was designed and developed according to a reported procedure, then purified by column chromatography. The receptor PEBD is a yellow-colored solid, air-stable, non-hygroscopic, and highly soluble in dimethyl sulfoxide (DMSO). A general synthetic procedure for the preparation of the receptor PEBD is given in **Scheme 1**.

The reaction of one equivalent of O-phenyl diamine with two equivalents of pyrene-1- carboxaldehyde in presence of glacial acetic acid as the catalyst gives a diimine structure followed by the formation of an imidazole ring. The receptor PEBD was obtained in a high yield. The compound was well characterized by

elemental analysis and spectroscopic studies including FT-IR, ^1H , ^{13}C , and ^{13}C DEPT- 135. Electronic spectra of the compound showed the absorption bands around 280 nm ($\pi \rightarrow \pi^*$) and 349 nm ($n \rightarrow \pi^*$). The Fourier-transform infrared spectra of the compound showed peaks in the range of 3042 cm^{-1} for aromatic C-H. The C=N band appeared at 1588 cm^{-1} and the peaks at 1350 cm^{-1} , 1277 cm^{-1} , and 1229 cm^{-1} correspond to different C-N stretching. Similarly, the aliphatic $-\text{CH}_2$ stretching is indicated by the peak at 2660 cm^{-1} , which is lower than the expected value, it might be due to the strong interaction between the nitrogen of the imidazole ring and carbon of the $-\text{CH}_2$ group. The presence of a negative peak at 46 ppm in ^{13}C DEPT- 135 indicates the methylene carbon in the compound, which proves the cyclized structure of the desired product. All of the characterization data is given in supplementary documents (**Fig. S1- S4**).

Fluorescence studies

Selectivity is an important parameter for a chemosensor because it measures the efficiency of a sensor. This study describes the ability of the receptor PEBD to detect Fe^{3+} ion in presence of 10- fold excess of various metal ions such as Co^{2+} , Cr^{3+} , Cu^{2+} , Fe^{2+} , Hg^{2+} , Pb^{2+} , K^+ , Ni^{2+} , Mg^{2+} , Cd^{2+} , Ca^{2+} , Mn^{2+} , Al^{3+} , and Zn^{2+} in the reaction medium. As depicted in **Fig. 1**, upon the addition of different cations in the receptor PEBD solution, only Fe^{3+} ions produce a significant fluorescence quenching at 440 nm. All other cations are inefficient to induce a large variation in the fluorescence intensity of receptor PEBD molecules. Furthermore, interference studies were also carried out. As shown in **Fig. 2**, the emission intensity of complex PEBD- Fe^{3+} was almost constant upon the addition of other cations. This suggested that the recognition process of Fe^{3+} was not affected by other cations. As mentioned earlier, the receptor PEBD was specific towards the detection of Fe^{3+} ion. Also, the response time of the receptor PEBD towards Fe^{3+} was studied (**Fig. S5**). The fluorescent intensity of the complex PEBD- Fe^{3+} becomes almost the same over different time intervals, suggesting that the formed complex is stable. To have a better understanding of the sensing mechanism and the limit of detection, fluorescence titration experiments were carried out (**Fig. 3a**). From **Fig. 3**, it was observed that the fluorescence emission of the receptor PEBD at 440 nm keeps decreasing upon the incremental addition of ($8 \times 10^{-5}\text{ M}$) aqueous Fe^{3+} solution (0-1.2 equivalents).

Fluorescence quenching was observed by the incremental addition of Fe^{3+} ion to the receptor solution. The fluorescence intensity of the receptor PEBD become constant after the addition of 1.2 equivalents of Fe^{3+} ion and further decrement was not observed even after the concentration of the Fe^{3+} ion increased in the solution. Since Fe^{3+} ion can quench the fluorescence intensity of the receptor PEBD, it can be suggested as a chemosensor for sensing iron (III) ions. The diminished fluorescence intensity could be attributed to the electron transfer from the receptor (lone pair of electrons in N-atoms) to the electron-deficient Fe^{3+} metal ion [21] since electron-deficient metal cations can act as a quencher in the sensor fluorescence [22].

Different chemosensors have been reported previously for the effective detection of Fe³⁺ ions [23-26]. The present study also compares different pyrene-based Fe³⁺ ion chemosensors with the present receptor PEBD. A calibration curve was drawn between concentration of Fe³⁺ ion and the fluorescence emission values, $y = -8.685 \times 10^{-7}x + 601.02$ ($R^2 = 0.9907$) (**Fig. 3a**). By using the equation $3\sigma/K$ the limit of detection was found to be 1.81 μM for the receptor PEBD which is less than the detection limits of previously reported chemosensors for Fe³⁺ ion [27-30], which is given in **Table S1** (supplementary data). According to a report by WHO, this is lower than the acceptable value of Fe³⁺ in drinking water. Similarly, the value of the quenching constant (K_b) was found to be $8.485 \times 10^3 \text{ M}^{-1}$ using the Benesi-Hildebrand equation constructed based on titration values (**Fig. 3b**). Therefore, the above results revealed that the receptor PEBD is a good candidate for the detection of Fe³⁺ ions and a standard curve was constructed with better linearity ($R^2=0.9907$) for the quantitative analysis of iron.

Fluorescence quenching was observed when the Fe³⁺ ion was added to the receptor PEBD, which proves the interaction of the Fe³⁺ ion with the receptor PEBD system. To confirm the structure of the receptor PEBD and the complex PEBD+ Fe³⁺ ESI-MS spectra were recorded (**Fig. 5**). The peaks at $m/z = 533.20$ and 699.16 are corresponding to the receptor PEBD and the complex [PEBD+ Fe³⁺ + Na⁺ + H₂O] respectively. The 1:1 ratio of receptor and Fe³⁺ ions were also confirmed with Job's diagram. The Job's plot was constructed based on the fluorescent titration values (**Fig. 4**). Since the point of intersection of the two straight lines was observed at mole fraction 0.5, the ratio of complex formation between the receptor PEBD and Fe³⁺ would be 1:1.

Computational DFT studies

To validate the experimental results, theoretical DFT calculations were carried out for both receptor PEBD and the complex PEBD-Fe³⁺ using the Gaussian 09 software with B3LYP/ 6-311G (d, p), LANL2DZ level of theory. As can be seen from the figure (**Fig. 6**), the HOMO-LUMO energy gap for the receptor PEBD and the complex PEBD-Fe³⁺ were found to be 0.1068 eV and 0.0484 eV respectively. The electronic distribution of receptor PEBD and complex PEBD-Fe³⁺ were not found similar. Since the obtained value is lowered by 0.0583 eV, the receptor PEBD shows high affinity towards Fe³⁺ ions and thereby forms a stable complex. The results obtained from the DFT studies described that the complex PEBD-Fe³⁺ has a lower HOMO-LUMO energy gap when compared to the receptor PEBD, which is an indication of a stabilized complex system. The receptor PEBD offers a suitable molecular structure to coordinate with the Fe³⁺ ions. The strong interaction between the receptor PEBD and Fe³⁺ ions induced distortion of the electronic structure of receptor PEBD, which results in the quenching of the fluorescent emission. Also, this HOMO-LUMO energy gap was used to evaluate the critical chemical reactivity parameters like softness, hardness (η), electronegativity (χ), the chemical potential (μ), electron-affinity (A), and ionization energy (I) (**Table S2**, supplementary data). These properties have been defined as follows [31].

$$\eta = (I-A)/2 \quad \mu = -(I+A)/2 \quad \chi = (I+A)/2$$

The values of I and A can be retrieved from HOMO and LUMO energies as $I = -E_{HOMO}$ and $A = -E_{LUMO}$ as per Janak theorem and Perdew et al. [32].

MEP analysis

Molecular electrostatic surfaces (MEP) analysis is useful for calculating the reaction behavior of compounds. MEP exposes important properties like size, shape, and variation of electron density while correlating it with a dipole moment, partial charges, electronegativity, and chemical reactivity sites located in the molecule [34]. ESP study helps the computation of organic chemists for analyzing drug-receptor and enzyme-substrate interactions along with H-bonding interactions [35].

A comparative view of molecular electrostatic maps (MEP) of the receptor PEBD is shown in **Fig. 7**. The MEP results describe the three-dimensional charge distribution within the receptor PEBD. Different interactions present in the molecules can be predicted by analyzing the positive and negative charged electrostatic potential regions in the compound. The blue coloured region or the surface with high electrostatic potential describes either the absence of electrons or the partial positive charge possessed by the compound. The electron-deficient region of the compound is indicated by a pale blue colour. The green colour shows zero potential or neutral, electron richness is well indicated by the yellow colour, and the low electrostatic potential or the electron abundance is represented by the red colour. The negative region of the MEP surface, which is indicated by the red and yellow colours is associated with the hetero atoms containing lone pairs of electrons, reveals the Lewis base region, and is liable to electrophilic attack or capable of coordination with metals. The slight blue colour can be seen near the aromatic protons of the pyrene ring and is evident in the absence of electron cloud there.

Molecular docking calculations

The crystal structure of CYP1A1 was retrieved from the protein data bank at a resolution of 2.60 Å. Blind docking calculations have been performed between the receptor PEBD and the complex using MGL tools 1.5.4 with Autogrid4 and Autodock4. The preparation of the protein was done by adding the polar hydrogen and Kollman charges after removing all the heteroatoms including water molecules. Rotatable bonds in the receptor PEBD were also introduced, then all the bonds were allowed to be rotatable. The receptor PEBD shows a high binding affinity towards the protein with a binding energy of -10.22 kcal/mol and is probably used as a candidate for therapeutic purposes. The amino acid residue SER 363 has hydrogen bond interaction with the receptor PEBD [SER 363 H(O): PEBD (N1)]. The nonbonding interactions of the receptor PEBD with the amino acid residues ILE-439, ARG-362, ALA-438, SER-363, LEU-365, and LYS-441 have shown in **Table S3** (supplementary data). **Fig. 8a** shows the interactions of the receptor PEBD with the active sites of the protein CYP1A1. The two-dimensional diagram for the corresponding interaction is also studied, which is exhibited in **Fig. 8b**. Also, **Fig. 9** demonstrates the 2D and 3D models of hydrogen bond interaction of the receptor PEBD with the protein CYP1A. The inhibition constant was observed as 32.42 nM. The docked poses were examined in terms of energy, H-bonding,

and the hydrophobic interplay between the receptor and the protein CYP1A. The present study reveals that the receptor PEBD can be considered a potent CYP1A1 protein inhibitor.

Conclusion

A pyrene-based fluorescent chemosensor for Fe(III) ion sensing has been developed and characterized successfully. The synthesis of chemosensor PEBD is quite simple and shows a high affinity towards Fe(III) ion in the presence of other metal ions. A linear calibration plot of $1/(I_0-I)$ against $1/Fe^{3+}$ was constructed with a correlation coefficient of 0.9982. The limit of detection value was calculated as 1.81 μ M using the equation $3\sigma/K$. The 1:1 molar ratio of the PEBD- Fe^{3+} complex was confirmed by Job's plot and the ESI-MS technique. Also, DFT studies have been performed to validate the experimental results. The quenching constant value was found as $8.485 \times 10^3 M^{-1}$ thereby confirming the good sensing property of PEBD towards Fe(III) ion. Furthermore, molecular docking studies were performed and revealed that the receptor (PEBD) can be considered a potent CYP1A1 protein inhibitor.

Declarations

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Author Declarations

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Conflicts of interest

The authors have no relevant financial or non-financial interests to disclose.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent to publish

Not applicable.

Availability of data and material

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Code availability

Not applicable.

Authors' contributions

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. Synthesis, characterization and application of the compound were done by Puthiyavalappil Rasin, Merlin Mary Mathew, Vipin Manakkadan and Vishnunarayanan Namboothiri Vadakkedathu Palakkeezhillam. The first draft of the manuscript was written by Puthiyavalappil Rasin and the final corrections were done by Anandaram Sreekanth and all the authors commented on the first version of the manuscript. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

References

1. Zhang H, Reynolds M (2019) Cadmium exposure in living organisms: A short review. *Sci. Total Environ.* 678:761–767
2. Bulck M Van, Sierra-Magro A, Alarcon-Gil J, et al (2019) Novel approaches for the treatment of alzheimer's and parkinson's disease. *Int. J. Mol. Sci.* 20
3. Peng T, Qi B, He J, et al (2020) Advances in the Development of Phosphodiesterase-4 Inhibitors. *J. Med. Chem.* 63:10594–10617
4. Pirzada RH, Javaid N, Choi S (2020) The roles of the NLRP3 inflammasome in neurodegenerative and metabolic diseases and in relevant advanced therapeutic interventions. *Genes (Basel).* 11
5. Peng Y, Chang X, Lang M (2021) Iron homeostasis disorder and alzheimer's disease. *Int. J. Mol. Sci.* 22
6. Nawaz H, Tian W, Zhang J, et al (2018) Cellulose-Based Sensor Containing Phenanthroline for the Highly Selective and Rapid Detection of Fe²⁺ Ions with Naked Eye and Fluorescent Dual Modes. *ACS Appl Mater Interfaces* 10:2114–2121. <https://doi.org/10.1021/acsami.7b17342>
7. Jiang C, Li Y, Wang H, et al (2020) A portable visual capillary sensor based on functional DNA crosslinked hydrogel for point-of-care detection of lead ion. *Sensors Actuators, B Chem* 307:.. <https://doi.org/10.1016/j.snb.2019.127625>

8. Alam P, Leung NLC, Zhang J, et al (2021) AIE-based luminescence probes for metal ion detection. *Coord. Chem. Rev.* 429
9. Hamed SA (2019) Neurologic conditions and disorders of uremic syndrome of chronic kidney disease: presentations, causes, and treatment strategies. *Expert Rev Clin Pharmacol* 12:61–90. <https://doi.org/10.1080/17512433.2019.1555468>
10. Woodman AG, Care AS, Mansour Y, et al (2017) Modest and severe maternal iron deficiency in pregnancy are associated with fetal anaemia and organ-specific hypoxia in rats. *Sci Rep* 7:. <https://doi.org/10.1038/srep46573>
11. Al-Fartusie FS, Mohssan SN Essential Trace Elements and Their Vital Roles in Human Body. <https://doi.org/10.22607/IJACS.2017.503003>
12. Listabarth S, König D, Vyssoki B, Hametner S (2020) Does thiamine protect the brain from iron overload and alcohol-related dementia? *Alzheimer's Dement* 16:1591–1595. <https://doi.org/10.1002/alz.12146>
13. Joseph J, Sajeesh AK, Nagashri K, et al (2021) Determination of ammonia content in various drinking water sources in Malappuram District, Kerala and its removal by adsorption using agricultural waste materials. In: *Materials Today: Proceedings*. Elsevier Ltd, pp 811–819
14. Berhanu AL, Gaurav, Mohiuddin I, et al (2019) A review of the applications of Schiff bases as optical chemical sensors. *TrAC - Trends Anal Chem* 116:74–91. <https://doi.org/10.1016/j.trac.2019.04.025>
15. Xu X, Liu S, Smith K, et al (2020) An overview on corrosion of iron and steel components in reclaimed water supply systems and the mechanisms involved. *J. Clean. Prod.* 276
16. Atsever N, Borahan T, Gülhan Bakırdere E, Bakırdere S (2020) Determination of iron in hair samples by slotted quartz tube-flame atomic absorption spectrometry after switchable solvent liquid phase extraction. *J Pharm Biomed Anal* 186:6–11. <https://doi.org/10.1016/j.jpba.2020.113274>
17. Ullah N, Mansha M, Khan I, Qurashi A (2018) Nanomaterial-based optical chemical sensors for the detection of heavy metals in water: Recent advances and challenges. *TrAC - Trends Anal Chem* 100:155–166. <https://doi.org/10.1016/j.trac.2018.01.002>
18. Yu L, Qiao Y, Miao L, et al (2018) Recent progress in fluorescent and colorimetric sensors for the detection of ions and biomolecules. *Chinese Chem Lett* 29:1545–1559. <https://doi.org/10.1016/j.ccllet.2018.09.005>
19. Shellaiah M, Wu YH, Singh A, et al (2013) Novel pyrene- and anthracene-based Schiff base derivatives as Cu²⁺ and Fe³⁺ fluorescence turn-on sensors and for aggregation induced emissions. *J Mater Chem A* 1:1310–1318. <https://doi.org/10.1039/c2ta00574c>

20. Basu A, Sarkar A, Maulik U (2020) Molecular docking study of potential phytochemicals and their effects on the complex of SARS-CoV2 spike protein and human ACE2. *Sci Rep* 10:1–15. <https://doi.org/10.1038/s41598-020-74715-4>
21. Li N, Xu Q, Xia X, et al (2009) A polymeric chemosensor for Fe³⁺ based on fluorescence quenching of polymer with quinoline derivative in the side chain. *Mater Chem Phys* 114:339–343. <https://doi.org/10.1016/j.matchemphys.2008.09.027>
22. Wang P, Meziani MJ, Fu Y, et al (2021) Carbon dots: Versus nano-carbon/organic hybrids- dramatically different behaviors in fluorescence sensing of metal cations with structural and mechanistic implications. *Nanoscale Adv* 3:2316–2324. <https://doi.org/10.1039/d1na00002k>
23. Alorabi AQ (2021) A new colorimetric chemosensor based on 1,3,4-oxadiazole derivative for the high selectivity and sensitivity of Fe³⁺ ion detection. *J Mol Struct* 132019. <https://doi.org/10.1016/j.molstruc.2021.132019>
24. Zhang R, Hu L, Xu Z, et al (2020) A highly selective probe for fluorescence turn-on detection of Fe³⁺ ion based on a novel spiropyran derivative. *J Mol Struct* 1204:127481. <https://doi.org/10.1016/j.molstruc.2019.127481>
25. Madhu P, Sivakumar P (2019) Selective and sensitive detection of Fe³⁺ ions using quinoline-based fluorescent chemosensor: Experimental and DFT study. *J Mol Struct* 1193:378–385. <https://doi.org/10.1016/j.molstruc.2019.05.044>
26. Senthil Murugan A, Vidhyalakshmi N, Ramesh U, Annaraj J (2018) In vivo bio-imaging studies of highly selective, sensitive rhodamine based fluorescent chemosensor for the detection of Cu²⁺/Fe³⁺ ions. *Sensors Actuators, B Chem* 274:22–29. <https://doi.org/10.1016/j.snb.2018.07.104>
27. Padghan SD, Puyad AL, Bhosale RS, et al (2017) A pyrene based fluorescent turn-on chemosensor: Aggregation-induced emission enhancement and application towards Fe³⁺ and Fe²⁺ recognition. *Photochem Photobiol Sci* 16:1591–1595. <https://doi.org/10.1039/c7pp00329c>
28. Bhorge YR, Tsai HT, Huang KF, et al (2014) A new pyrene-based Schiff-base: A selective colorimetric and fluorescent chemosensor for detection of Cu(II) and Fe(III). *Spectrochim Acta - Part A Mol Biomol Spectrosc* 130:7–12. <https://doi.org/10.1016/j.saa.2014.03.110>
29. Zhang W, Luo Y, Zhou Y, et al (2020) A highly selective fluorescent chemosensor probe for detection of Fe³⁺ and Ag⁺ based on supramolecular assembly of cucurbit[10]uril with a pyrene derivative. *Dye Pigment* 176:108235. <https://doi.org/10.1016/j.dyepig.2020.108235>
30. Guo Y, Wang L, Zhuo J, et al (2017) A pyrene-based dual chemosensor for colorimetric detection of Cu²⁺ and fluorescent detection of Fe³⁺. *Tetrahedron Lett* 58:3951–3956. <https://doi.org/10.1016/j.tetlet.2017.08.078>

31. Adole VA (2021) Computational Chemistry Approach for the Investigation of Structural, Electronic, Chemical and Quantum Chemical Facets of Twelve Biginelli Adducts. *J Appl Organomet Chem* 1:29–40
32. Doust Mohammadi M, Abdullah HY (2021) The adsorption of bromochlorodifluoromethane on pristine, Al, Ga, P, and As-doped boron nitride nanotubes: A study involving PBC-DFT, NBO analysis, and QTAIM. *Comput Theor Chem* 1193:.. <https://doi.org/10.1016/j.comptc.2020.113047>
33. Ben El Ayouchia H, Bahsis L, Anane H, et al (2018) Understanding the mechanism and regioselectivity of the copper(i) catalyzed [3 + 2] cycloaddition reaction between azide and alkyne: A systematic DFT study. *RSC Adv* 8:7670–7678. <https://doi.org/10.1039/c7ra10653j>
34. Bhat MA, Lone SH, Butcher RJ, Srivastava SK (2018) Theoretical and experimental investigations into structural, electronic, molecular and biological properties of 4-(3-chlorophenyl)-1-(3-chloropropyl) piperazin-1-ium chloride. *J Mol Struct* 1168:242–249. <https://doi.org/10.1016/j.molstruc.2018.05.019>
35. Lone SH, Bhat MA, Lone RA, et al (2018) Hemisynthesis, computational and molecular docking studies of novel nitrogen containing steroidal aromatase inhibitors: Testolactam and testololactam. *New J Chem* 42:4579–4589. <https://doi.org/10.1039/c8nj00063h>

Scheme

Please see the Supplementary Files for the Scheme 1 and 2.

Figures

Figure 1

(a) Fluorescence intensity pattern of receptor PEBD (1×10^{-5} M) in the presence of different cations (10×10^{-5} M) in DMSO/water (95/5, v/v) solution, **(b)** Changes in the fluorescence intensity of receptor PEBD in the presence of various metal ions in DMSO/water (95/5, v/v) solution ($\lambda_{em}=440$ nm, $\lambda_{ex}=280$ nm)

Figure 2

(a) Interference study of the PEBD- Fe^{3+} sensor over various metal ions in DMSO/water (95/5, v/v) solution **(b)** the fluorescence spectra of PEBD with the incremental addition of Fe^{3+} in DMSO/water (95/5, v/v) solution ($\lambda_{em}=440$ nm, $\lambda_{ex}=280$ nm)

Figure 3

(a) A plot of emission intensities of receptor PEBD against different Fe^{3+} ion concentrations, (b) Benesi-Hildebrand plot of $1/(I_0-I)$ versus $1/[\text{Fe}^{3+}]$ based on 1:1 stoichiometry between receptor PEBD- Fe^{3+} complex ($\lambda_{\text{em}}=440$ nm, $\lambda_{\text{ex}}=280$ nm)

Figure 4

Job's diagram of receptor PEBD- Fe^{3+} complex in DMSO/water (95/5, v/v) solution.

Figure 5

ESI-MS spectrum of receptor PEBD- Fe^{3+} complex

Figure 6

Relevant frontier molecular orbital profiles of receptor PEBD and PEBD- Fe^{3+} complex

Hardness (η) which is a measure of resistance to change the electronic environment of the system was found to be 0.0534 eV for the receptor PEBD and 0.0242 eV for PEBD- Fe^{3+} . Chemical potential is the escaping ability of electrons from an equilibrium system was -0.1454 eV and -0.1853 eV for the receptor PEBD and complex PEBD- Fe^{3+} respectively. The global electrophilicity index (ω), a global reactivity index that is related to η and μ , and was first introduced by Parr et al. [33]. It is the amount of the stabilization in energy achieved when the system gets an additional electronic charge from the environment and is given by $\omega = \mu^2/\eta$. The corresponding values for the receptor PEBD and the complex PEBD- Fe^{3+} were found as 0.3959 eV and 1.4188 eV respectively.

Figure 7

The MEP of receptor PEBD calculated using B3LYP/6-311G (d, p) basis set.

Figure 8

(a) Binding mode of receptor PEBD at the active site of CYP1A1 protein, (b) the two-dimensional representation of receptor PEBD at the active site of CYP1A1 protein

Figure 9

Molecular docking (a) 2-D and (b) 3-D models demonstrate the hydrogen bond interaction of receptor PEBD with the amino acid Ser363(B) of the protein CYP1A1

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [scheme1.jpg](#)
- [scheme2.jpg](#)
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