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Imatinib intermediate as a two in one dual channel sensor for the recognition of  $Cu^{2+}$  and  $I^-$  ions in aqueous media and its practical applications<sup>†</sup>

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An imatinib intermediate, 6-methyl-*N*-[4-(pyridin-3-yl)pyrimidin-2-yl]benzene-1,3-diaminepyridopyrimidotoluidine (**PPT-1**), was developed for the colorimetric sensing of  $Cu^{2+}$  ions in aqueous solution. With  $Cu^{2+}$ , the receptor **PPT-1** showed a highly selective naked-eye detectable color change from colorless to red over the seventy other tested cations. The colorimetric sensing ability of **PPT-1** was successfully utilized in the preparation of test strips and supported silica for the real samples analysis to detect  $Cu^{2+}$  ions from 100% aqueous environment. Moreover, the iodide-sensing ability of receptor **PPT-1** was explored among the ten examined anions.

# Introduction

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Copper, the third most abundant transition element in humans, plays an important role in various physiological processes such as hemoglobin biosynthesis, bone development, dopamine production, and nerve function regulation.<sup>1-4</sup> Similarly, Cu<sup>2+</sup> ions play critical role as catalytic cofactors for a variety of metalloenzymes such as copper-zinc superoxide dismutases, lysyloxidase, cytochrome c oxidase, and tyrosinase.<sup>5-8</sup> Apart from the biotic significances, copper is extensively used in various industrial, pharmaceuticals and agricultural purposes such as for making alloys, electrical wires, machine parts, batteries and fertilizers.9 Under normal condition, the average concentration of copper in the blood should not exceed 100-150 µg dL<sup>-1</sup>, because an increased concentration of copper by any means in the body can cause improper cellular functions and progression of various diseases.<sup>10</sup> Excess accumulation of copper in humans because of the widespread utilization leads to serious detrimental effects, including neurodegenerative diseases such as Alzheimer's disease, Menkes disease, Wilson's disease, prion disease, amyotrophic

sclerosis, metabolism and inflammatory lipid disorders.<sup>7,8,11–13</sup> Therefore, there is a need to develop newer technologies and methods for the qualitative and quantitative detection of copper. In the past literatures, different analytical methods are developed for the detection of Cu<sup>2+</sup>, namely, inductively coupled plasma detectors, quantum-dot-based assay, fluorescence anisotropy, surface-plasmon resonance detector, and electrochemical and fluorescent sensors<sup>14,15</sup> These technologies can detect Cu<sup>2+</sup> ion selectively with high sensitivity but need highly sophisticated expensive instrumentation. Although fluorescent sensor can have better sensitivity and selectivity with fast response, literature reports tell that the same is not well suited particularly for paramagnetic cations like Cu2+ due to their ability to act as fluorescent quencher, which rendered low signal output. Therefore, fluorescent sensors are sometimes less advantageous for the recognition of Cu<sup>2+</sup>, and they give false spectrometric response.<sup>16,17</sup> Alternatively, the absorption-based colorimetric chemosensor can be explored because of the distinct visual color change with analyte due to charge transfer band for easy detection by naked-eye.

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On the other hand, considerable research has been focused on the selective recognition of anions in water for monitoring environmental pollution, medicinal diagnostic and the analysis of biological samples.<sup>18</sup> Among the various biologically important anions, iodide plays imperative roles in several biological activities such as thyroid gland function and neurological activity. In addition, elemental iodine has been used to synthesize drugs, fine chemicals, and dyes that can be applied in the chemistry, biology and food disciplines.<sup>19,20</sup> Radioactive

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isotope of iodine is used in medicines and also in analytical chemistry. The iodide content of urine and milk is often required to provide information for nutritional, metabolic and epidemiological studies of thyroid disorder.<sup>21,22</sup> Due to the important roles played by iodide in day to day life, there is also a need for developing simple analytical method to detect iodide in aqueous system. Similar to cations, several methods in literatures are available for iodide detection such as ICP-MS, capillary electrophoresis and iodide-selective electrode.<sup>23,24</sup> Recently, fluorescent sensors have been extensively developed with high sensitivity and selectivity for the detection of iodide.25-28 However, very few colorimetric chemosensors are available for the detection of iodide in aqueous system.<sup>28-30</sup> Thus, there is a significant demand for the expansion of synthetic receptors capable of selectively recognizing iodide over the other important anions in aqueous system.

Recently, the design and synthesis of imatinib (a derivative 2-phenylamino-pyrimidine) derivatives has increased of immensely due to their anticancer applications. Imatinib is one of the largest selling anticancer drugs and tyrosine kinase inhibitor and is used mostly for the treatment of chronic myeloid leukemia and gastrointestinal stromal tumors.31,32 Imatinib is synthesized by a multistep synthetic pathway and its synthesis goes through a series of intermediates. To date, there has been no report on the utilization of imatinib intermediates as a chemosensor. Moreover, several chemosensors for recognition of Cu<sup>2+</sup> or iodide are reported, but very few of them are able to recognize  $Cu^{2+}$  and  $I^-$  simultaneously in aqueous system (Table S1<sup>†</sup>). Herein, as a part of our ongoing efforts in the field of sensing<sup>33-36</sup> and to address the above stated problems, we have successfully developed an imatinib intermediate (PPT-1) for the highly selective and sensitive colorimetric sensing of Cu<sup>2+</sup> and iodide ions from 100% aqueous solution. Furthermore, the receptor PPT-1 was successfully utilized in the development of test strips and supported silica for the detection of Cu<sup>2+</sup> ions.

## **Experimental**

## Materials and instrumentation

Unless otherwise stated, all the chemicals used for the synthesis of **PPT-1** were of AR grade and were purchased either from S. D. Fine Chemicals or Sigma Aldrich depending on their availability. All the solvents were of spectroscopic grade and were used without further treatment. The aqueous stock solutions of cations and anions of concentration  $1 \times 10^{-2}$  mol L<sup>-1</sup> were prepared from their corresponding salt, *i.e.* AgClO<sub>4</sub>, Al(ClO<sub>4</sub>)<sub>3</sub>·9H<sub>2</sub>O, Ba(ClO<sub>4</sub>)<sub>2</sub>, Ca(NO<sub>3</sub>)<sub>2</sub>·4H<sub>2</sub>O, Cd(ClO<sub>4</sub>)<sub>2</sub>. H<sub>2</sub>O, Co(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cr(ClO<sub>4</sub>)<sub>3</sub>·6H<sub>2</sub>O, Fe(ClO<sub>4</sub>)<sub>2</sub>·xH<sub>2</sub>O, HgCl<sub>2</sub>, LiBr, Mg(ClO<sub>4</sub>)<sub>2</sub>, Mn(ClO<sub>4</sub>)<sub>2</sub>·H<sub>2</sub>O, Ni(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Fe(ClO<sub>4</sub>)<sub>3</sub>·H<sub>2</sub>O, Pb(ClO<sub>4</sub>)<sub>2</sub>·3H<sub>2</sub>O, Zn(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, Cu(ClO<sub>4</sub>)<sub>2</sub>·6H<sub>2</sub>O, (*n*-Bu)<sub>4</sub>NOAc, (*n*-Bu)<sub>4</sub>NBr, (*n*-Bu)<sub>4</sub>NCl, (*n*-Bu)<sub>4</sub>NCO<sub>4</sub>, (*n*-Bu)<sub>4</sub>NNO<sub>3</sub>, and (*n*-Bu)<sub>4</sub>NI. The stock solution of **PPT-1** (1 × 10<sup>-3</sup> mol L<sup>-1</sup>) was prepared by dis-

solving an accurately weighed **PPT-1** in CH<sub>3</sub>CN, and then diluted to  $3 \times 10^{-5}$  mol L<sup>-1</sup> with CH<sub>3</sub>CN-H<sub>2</sub>O (40 : 60) mixed solvent.

The <sup>1</sup>H and <sup>13</sup>C-NMR spectra were recorded on a Bruker 400 MHz Avance II multinuclear probe NMR spectrometer at ambient temperature in CDCl<sub>3</sub> with TMS as internal standard and the chemical shifts were reported in ppm. The electron spray mass spectra were recorded on a Q-TOP micromass (LCMS) mass spectrometer. The IR spectra were recorded on a Perkin Elmer spectrophotometer as KBr discs and the IR bands are expressed in frequency (cm<sup>-1</sup>). Absorption spectra were recorded on a Perkin Elmer U 3900 Co, USA UV/Visible double beam spectrophotometer. The purity of the compound and progress of the reaction were monitored by means of thin layer chromatography (TLC). Pre-coated silica gel 60 F<sub>254</sub> (Merck) on alumina plate  $(7 \times 3 \text{ cm})$  was used and visualized by using either iodine or short UV/Visible lamp. Melting points, which are uncorrected, were recorded on the celsius scale by open capillary method.

Synthesis of N-(5-amino-2-methylphenyl)-4-(3-pyridinyl)-2pyrimidineamine (PPT-1). The receptor PPT-1 was synthesized by adopting the known literature procedure<sup>31,37</sup> as shown in Scheme 1. A 100 mL three-necked, round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and thermometer socket was charged with N-(2-methyl-5-nitrophenyl)-4-(pyridin-3-yl)pyrimidin-2-amine (3, 0.307 g, 1 mmol) [ESI<sup>†</sup>], hydrazine mono hydrate (0.154 g of 65% solution in water, 2 mmol), FeCl<sub>3</sub> (2.1 mg, 0.013 mmol), active carbon (0.02 g) and water (40 mL). The reaction mass was heated to about 80 °C for 6-8 h, and the reaction progress was monitored by TLC. After completion of reaction, the reaction mixture was cooled to room temperature. Insoluble materials were filtered off, and the filtrate was extracted with ethyl acetate (10 mL  $\times$  5). The combined organic layers were washed with brine and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The solvent was removed under reduced pressure in vacuo to obtained the product as yellow crystals (yield: 80%); m.p. 140-142 °C; IR (cm<sup>-1</sup>) [KBr]: 3360–33050, 2940, 2860, 1633, 1602; mass



Scheme 1 Synthesis of imatinib intermediate *i.e.* 6-methyl-*N*1-(4-(pyridin-3-yl)pyrimidin-2-yl)benzene-1,3-diamine (PPT-1).

[ESI, 70 eV] m/z (%): 279 (26), 278 (65); <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>,  $\delta$  ppm): 2.07 (3H, bs, CH<sub>3</sub>), 4.87 (2H, s, NH<sub>2</sub>), 6.33–6.35 (1H, dd, J = 4 Hz, ArH), 6.79–6.80 (1H, d, J = 4 Hz, ArH), 6.86–6.88 (1H, d, J = 8 Hz, ArH), 7.36–7.38 (1H, d, J = 12 Hz, ArH), 7.53–7.56 (1H, dd, J = 4 Hz, ArH), 8.40–8.43 (1H, m, ArH), 8.46–8.48 (1H, d, J = 8 Hz, ArH), 8.69–8.71 (2H, m, ArH), 9.25 (1H, s, NH); <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>,  $\delta$  ppm): 17.1, 99.8, 103.6, 106.2, 118.3, 121.4, 129.8, 131.2, 134.6, 142.2, 144.3, 146.9, 147.2, 155.6, 160.8, 169.7. Anal. calcd for C<sub>16</sub>H<sub>15</sub>N<sub>5</sub>: C, 69.29; H, 5.45; N, 25.25. Found: C, 69.42; H, 5.43; N, 25.14 (Fig. S1 and S2†).

### Computational study

The structural optimization of **PPT-1** and its host–guest complexes with the Cu<sup>2+</sup> and I<sup>–</sup> was performed using the computer program Gaussian 09W<sup>38</sup> by applying the density functional theory (DFT) method. All the DFT calculations were performed in the gas phase with a hybrid functional B3LYP (Becke's three parameter hybrid functional using the LYP correlation functional) using the basis sets 6-31G(d,p) for C, H, N atoms and LANL2DZ for Cu, I atoms.

# **Results and discussion**

## Sensing of Cu<sup>2+</sup> by PPT-1

The selective and sensitive detection of  $Cu^{2+}$  ions in water can be seen from the observed color change of **PPT-1** solution from colorless to dark red (Fig. 1). To perform these naked-eye experiments, 5 equivalents of various cations (30 µL, 1 ×  $10^{-2}$  M, in H<sub>2</sub>O) including  $Cu^{2+}$  ions were added to the solution of **PPT-1** (2 mL, 3 ×  $10^{-5}$  M) in CH<sub>3</sub>CN–H<sub>2</sub>O (40:60, v/v). No significant color change was observed with other cations, which reflects the ability of **PPT-1** to recognize  $Cu^{2+}$  ions selectively from aqueous solutions.

The UV-Vis absorption spectra were recorded to gain more insight into the chemosensing mechanism and binding behavior of **PPT-1** towards different metal cations (Fig. 2). The receptor **PPT-1** exhibited three peaks at 240, 270 and 305 nm in CH<sub>3</sub>CN–H<sub>2</sub>O (40:60, v/v). The peaks at 240 nm and 270 nm were assigned due to the  $\pi \rightarrow \pi^*$  electronic transition whereas the maxima at 305 nm appeared due to the  $n \rightarrow \sigma^*$  or  $n \rightarrow \pi^*$  transition. Upon addition of Cu<sup>2+</sup> ions (30 µL, 1 × 10<sup>-2</sup>, in H<sub>2</sub>O) to the **PPT-1** solution (2 mL, 3 × 10<sup>-5</sup> M) in CH<sub>3</sub>CN–H<sub>2</sub>O (40:60, v/v), two new peaks at 223 nm (a blue-shift of 17 nm

from 240 nm) and a broad peak with maxima at 358 nm (a red-shift of 53 nm from 305 nm) appeared. The spectral shifts accompanied with the color change clearly delineated the formation of a complex species between **PPT-1** and Cu<sup>2+</sup>. However, other cations  $(Ag^+, Al^{3+}, Ba^{2+}, Ca^{2+}, Cd^{2+}, Co^{2+}, Cr^{3+}, Cu^{2+}, Fe^{2+}, Fe^{3+}, Li^+, Mg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zr^{2+}, Zn^{2+}$  and  $Hg^{2+}$ ) showed no remarkable changes between 330 and 400 nm. Furthermore, the competitive experiments inferred that the selective recognition of Cu<sup>2+</sup> ions was slightly or not influenced in the presence of various interfering cations in 100% aqueous medium (Fig. S3†).

The UV-Vis absorption titration of **PPT-1** with Cu<sup>2+</sup> was performed to determine the various analytical parameters such as binding ability, stoichiometry, and detection limit. The changes in UV-Vis spectrum of PPT-1 upon successive incremental addition of Cu<sup>2+</sup> ions is shown in Fig. 3. Upon addition of 1–5 equivalents of Cu<sup>2+</sup> ions to **PPT-1**, the absorbance peaks at 223 nm and 358 nm were increased sharply which may be attributed to the interaction of Cu<sup>2+</sup> ions with PPT-1. Furthermore, to determine the stoichiometry of the formed complex between **PPT-1** and Cu<sup>2+</sup>, Job's plot (Fig. S4<sup>†</sup>) and mole ratio plot (Fig. S5<sup>†</sup>) methods were employed and the 1:1 stoichiometry was found for the **PPT-1**·Cu<sup>2+</sup> complex formed in solution. To confirm the mechanism of binding of Cu<sup>2+</sup> with PPT-1, we carried out <sup>1</sup>H-NMR titrations experiments, in which spectra were recorded by adding incremental amounts of copper perchlorate (0, 0.2, 0.5, 1.0 equiv.) to the solution of **PPT-1** in CDCl<sub>3</sub>. Addition of paramagnetic Cu<sup>2+</sup> affects the NMR resonance frequency of protons, which are close to the binding sites of the ligand. It was found that the peak corresponding to  $-NH_2$  protons at  $\delta = 3.641$  ppm disappears immediately on addition of 0.2 equivalents of  $Cu^{2+}$ . Furthermore, additions of Cu<sup>2+</sup> results in overall broadening of all the peaks of the compound (Fig. S6<sup>†</sup>). The disappearance of peak due to -NH2 proton on addition of 0.2 equivalents of Cu<sup>2+</sup> confirms the deprotonation and binding of **PPT-1** with copper. The broadening of peaks on addition of more amounts of copper is expected due to the paramagnetic nature of Cu<sup>2+</sup>. A more direct evidence for the formation of 1:1 complex of PPT-1 with Cu<sup>2+</sup> is obtained from the HR-MS analysis of a mixture of **PPT-1** and copper perchlorate in acetonitrile (Fig. S7<sup>†</sup>). A MS peak observed at 414.6850 (calc. = 414.0388) corresponds to  $[(PPT-1-2H + Cu)\cdot 2H_2O + K + H]$ . Furthermore, the binding or association constant for the complexation of PPT-1 and Cu<sup>2+</sup> was obtained from Benesi-Hildebrand plot



Fig. 1 Naked-eye detection of Cu<sup>2+</sup> ion by PPT-1 in the presence of other metal cations under visible or sunlight.



Fig. 2 Absorption spectra of PPT-1 (3  $\times$  10<sup>-5</sup> M) in CH<sub>3</sub>CN-H<sub>2</sub>O (40 : 60, v/v) upon addition of 5 equivalents of various metal cations (1  $\times$  10<sup>-2</sup> M, in H<sub>2</sub>O).



Fig. 3 UV-Vis absorption titration spectra of PPT-1 (3  $\times$  10<sup>-5</sup> M) in CH<sub>3</sub>CN-H<sub>2</sub>O (40:60) with the addition of 1–5 equivalents of Cu<sup>2+</sup> ions (1  $\times$  10<sup>-3</sup> M, in H<sub>2</sub>O).



The limit of detection (LOD) and limit of quantification (LOQ) of the receptor **PPT-1** was calculated for  $Cu^{2+}$  ions. To calculate the relative standard deviation, the absorption measurements of ten blank samples were taken. The calibration curves (absorbance *vs.*  $[Cu^{2+}]$ ) were plotted (Fig. S8†), and then the obtained slope was used to calculate LOD and LOQ values. According to the IUPAC definition, the LOD and LOQ was calculated using the standard relationship *i.e.* LOD =  $(3.3 \times \text{standard deviation})/\text{slope}$  and LOQ values of **PPT-1** for  $Cu^{2+}$  ions are 0.54  $\mu$ M and 1.6  $\mu$ M, respectively. These observed LOD and LOQ limits are far superior to the allowed limit of  $Cu^{2+}$  for human beings.

## Analytical applications of PPT-1

In order to ensure the analytical applicability for the detection of  $Cu^{2+}$ , **PPT-1** loaded test strips and silica gel were prepared.



Fig. 4 Benesi–Hildebrand plot of  $1/[\Delta A]$  against  $1/[Cu^{2+}]$ .



Fig. 5 Practical application of PPT-1 for detection of  $Cu^{2+}$  by test strip method.

The desired test strips were prepared by soaking small strips of cellulose paper (Whatman) in the solution of **PPT-1** ( $1 \times 10^{-2}$  M) in acetonitrile and dried in air. When the strip was dipped in aqueous solution of Cu<sup>2+</sup> ( $1 \times 10^{-3}$  M), the colorless strips sharply turned into dark brown color (Fig. 5 and ESI video†).

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Fig. 6 Practical application of PPT-1 for detection of  $Cu^{2+}$  by silical support method.

The rapid color change of the test strip in solution clearly inferred the practical application of **PPT-1** for the qualitative detection of Cu<sup>2+</sup> in aqueous medium.

Moreover, the qualitative recognition of  $Cu^{2+}$  by **PPT-1** was worked on a solid support (Fig. 6 and ESI video†). The silica gel (60–120 mesh, 10 g, colorless) was first treated with **PPT-1** (in methanol, 50 mL,  $1 \times 10^{-2}$  M), and then dried to get a significantly faint yellow color silica gel loaded with the receptor on the surface. When it was treated with 10 mL aqueous solution of  $Cu^{2+}$  ( $A = 1 \times 10^{-3}$  M,  $B = 1 \times 10^{-4}$  M,  $D = 1 \times 10^{-5}$  M,  $E = 1 \times 10^{-6}$  M), the faint yellow color promptly turned to a dark brown color (ESI video†), whereas in bottle 'C', the untreated silica was added into the aqueous solution of  $Cu^{2+}$ ions ( $1 \times 10^{-2}$  M). The prompt color change of the solid silica gel was observed only in the presence of silica loaded with **PPT-1**, which clearly inferred the practical application of **PPT-1** for the qualitative detection of  $Cu^{2+}$  in aqueous medium.

## Sensing of I<sup>-</sup> by PPT-1

The binding profiles of **PPT-1** toward various anions were investigated by UV-Vis absorption spectroscopy. Except I<sup>-</sup>, the introduction of various anions of concentration  $1 \times 10^{-2}$  M in water did not cause any significant change in the absorption profile of **PPT-1** in CH<sub>3</sub>CN-H<sub>2</sub>O (40:60, v/v) (Fig. 7). Upon



Fig. 7 UV-Vis spectral changes of PPT-1 (3  $\times$  10<sup>-5</sup> M) in CH<sub>3</sub>CN-H<sub>2</sub>O (40:60) upon addition of 5 equivalents of TBA salts of different anions (1  $\times$  10<sup>-2</sup> M, in H<sub>2</sub>O).



**Fig. 8** UV-Vis spectral titration of **PPT-1** (3 × 10<sup>-5</sup> M) in CH<sub>3</sub>CN-H<sub>2</sub>O (40:60) upon incremental addition of 1–5 equivalents of iodide (1 × 10<sup>-3</sup> M, in H<sub>2</sub>O). Inset: Mole ratio plot/change in absorption spectra ( $\Delta A$ ) as a function of mole equivalents of I<sup>-</sup> ions.

addition of  $I^-$  ions to the solution of **PPT-1**, a new intense absorption band at 232 nm was observed. Furthermore, the selective and sensitive detection of  $I^-$  in the presence of other competing anions from aqueous solutions was also free from the interference of the other anions (Fig. S8†). The above results clearly indicate that the receptor **PPT-1** recognizes  $I^-$  selectively over other anions.

The recognition profile and mode of binding of PPT-1 with I<sup>-</sup> was illustrated by performing the absorption titration experiments. Upon continuous addition of I<sup>-</sup>  $(1 \times 10^{-3} \text{ M}, \text{ in H}_2\text{O})$ from 1-5 equivalents to the solution of PPT-1 in CH<sub>3</sub>CN-H<sub>2</sub>O (40:60, v/v), the intensity of the band at 232 nm was successfully enhanced due to the formation of pseudo cavity of complementary size by PPT-1 to make electrostatic and/or hydrogen bonding with I<sup>-</sup> (Fig. 8). To confirm the mechanism of binding of PPT-1 with I<sup>-</sup>, we carried out <sup>1</sup>H-NMR titration experiments, in which spectra were recorded by adding varying equivalents of tetrabutylammonium iodide (0, 0.2, 1.0, 4.0, 6.0) to the solution of **PPT-1** in CDCl<sub>3</sub>. It was found that the peak corresponding to  $-NH_2$  protons at  $\delta = 3.641$  ppm undergoes broadening accompanied by a small shift to  $\delta$  = 3.651 ppm (Fig. S10<sup>†</sup>). The broadening of the peak suggests that the I<sup>-</sup> sensing is mainly due to hydrogen bonding. To confirm the stoichiometry of binding, we carried out HR-MS studies on acetonitrile solutions of PPT-1 in presence of Ianions. Observation of a MS peak at 980.6509 (calc. 980.4284), corresponding to the species  $[2(PPT-1) + I + TBA + K + H_2O]$ , confirms the 2:1 binding stoichiometry (Fig. S11<sup>†</sup>). To get further comprehension concerning the binding stoichiometry, Job's plot and mole ratio plot methods were employed. The Job's plot (Fig. S12<sup>†</sup>) and mole ratio plot (Fig. 8, inset) clearly delineated the formation of host-guest complex between PPT-1 and iodide in 2:1 binding stoichiometry. The association constant or binding constant for the complexation of **PPT-1**·I<sup>-</sup> was calculated from Benesi-Hildebrand plot (Fig. 9) and was found to be 5687 M<sup>-1</sup>. This high value of binding constant designates the strong binding interactions between PPT-1 and I<sup>-</sup>. In order to check the applicability of receptor

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Fig. 9 Benesi-Hildebrand plot of  $1/[\Delta A]$  against  $1/[I^-]$  for binding constant.

**PPT-1**, we have calculated the detection limit and quantification limit for I<sup>-</sup> ions. From the straight line regression obtained by the graph plotted between absorbance *vs.* concentration of I<sup>-</sup> ions (Fig. S13<sup>†</sup>), the estimated limit of detection (LOD) and limit of quantification (LOQ) for I<sup>-</sup> was found to be 0.22 µM and 6.7 µM, respectively.

### Theoretical results

The structural optimization of the receptor **PPT-1** and its **PPT-1**·Cu<sup>2+</sup>/I<sup>-</sup> complexes along with the intermolecular charge transfer (ICT) process that occurred during the encapsulation of analytes (Cu<sup>2+</sup> and I<sup>-</sup>) by **PPT-1** was investigated in the gas phase by applying the exchange-correlation function B3LYP, and the basis sets 6-31G(d,p) (for C, H and N atoms) and LANL2DZ (for Cu and I atoms). The optimized structure of the receptor **PPT-1** and its **PPT-1**·Cu<sup>2+</sup>/I<sup>-</sup> complexes was shown in Fig. 10. On complexation of **PPT-1** with Cu<sup>2+</sup> and I<sup>-</sup>, the calculated interaction energy ( $E_{int} = E_{complex} - E_{receptor} - E_{Cu<sup>2+</sup>/I<sup>-</sup>}$ ) was

lowered respectively by -322.91 kcal mol<sup>-1</sup> and -9.49 kcal mol<sup>-1</sup>, which indicates the formation of stable complexes. The receptor PPT-1 organized itself by a slight molecular twist to encapsulate Cu<sup>2+</sup> preferably through the pyridine-N and amine-N atoms. Since the ICT band in PPT-1 originates from the electron donation from HOMO, localized on the pyrimidine, amino and sp<sup>2</sup>-nitrogen substituents to the LUMO, localized on the pyridine ring (Fig. 11), the considerable perturbation in this band on the addition of Cu<sup>2+</sup> can be ascribed to the stabilization of LUMO and a consequent decrease in the energy gap between HOMO and LUMO. The lowering of energy gap resulted in the observed bathochromic or red-shift of 53 nm in the ICT band and consequently the perceptible change in color from colorless to dark red. On the other hand, the protons at the amine groups (-NH2 and -NH-) can act as both hydrogen bond donor and acceptor, which makes an interesting combination for the recognition of iodide anion. The analysis of the molecular electrostatic potential (MEP) map of PPT-1 (Fig. 10b) also indicates that the two most positive regions shown in blue color are located above the amine protons. On interaction with iodide ion, molecular-twist was observed in the PPT-1 molecules, which created a pseudo cavity of complementary size to encapsulate iodide ion through multiple weak intermolecular hydrogen bonds. Furthermore, the HOMO and LUMO diagrams of **PPT-1** and (**PPT-1**)<sub>2</sub>·I<sup>-</sup> indicate the internal charge transfer occurred during the iodide recognition between the receptor and iodide ions (Fig. 11).

# Conclusion

In summary, we have successfully developed an imatinib intermediate **PPT-1** as a chemosensor for the recognition of  $Cu^{2+}$ 



Fig. 10 DFT computed optimized structure of the receptor (a) PPT-1 with its (b) molecular electrostatic potential (MEP), (c) PPT-1· $Cu^{2+}$  and (d) (PPT-1)<sub>2</sub>·I in the gas phase.



Fig. 11 DFT computed LUMO and HOMO diagrams of (a) receptor PPT-1, (c) alpha and (b) beta orbitals of PPT-1·Cu<sup>2+</sup>, and (d) (PPT-1)<sub>2</sub>·I in the gas phase.

and  $I^-$  from 100% aqueous media with high selectivity and sensitivity.

The recognition of  $Cu^{2+}$  was confirmed by remarkable color change from colorless to dark red with the appearance of a new charge transfer band. The remarkable colorimetric sensing of **PPT-1** confirmed a 1:1 (**PPT-1**· $Cu^{2+}$ ) binding model with the detection limit down to 0.54 µM. Moreover, **PPT-1** can be applied to detect  $Cu^{2+}$  in the aqueous media by naked-eye using test strip and silica support methods, whereas, the iodide ions did not bring any color change of **PPT-1**, but resulted a remarkable spectroscopic response by giving a new intense peak in the absorption spectrum at 232 nm. With **PPT-1**, the iodide ions can be detected up to 0.22 µM in aqueous solution. The good selectivity of chemosensor **PPT-1** for the detection of  $Cu^{2+}$  and **I**<sup>-</sup> from pure aqueous medium can open new doors for many practical applications in chemical, environmental and biological systems.

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