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Notes

Binding interaction of a piperazinylquinoline derivative with β-cyclodextrin and Cd^{2+} ions

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Cd^{2+} ion sensing by 3-methyl-2-(piper-azin-l-yl)quinoline using fluorescence spectroscopy is reported. The host-guest complex formation of the compound with β-cyclodextrin is studied using UV-visible absorption, fluorescence, and 2-dimensional ROESY spectroscopic methods. The stoichiometry and the mode of binding of the compound with the host molecule are reported. The 1:1 Cd^{2+} complexation of the compound is effected on encapsulation by β-cyclodextrin.

Keywords: Analytical chemistry, Host-guest complexation, Chemosensors, Encapsulation, Fluorescence spectroscopy, Cadmium, Piperazinylquinolines, β-Cyclodextrin

Cadmium is a highly toxic heavy metal which affects the environmental health through discharge from industry and agriculture.[1,2] Several selective and sensitive fluorescence sensors have been designed and synthesized for Cd^{2+} ions.[3-9] However, the response of fluorescent chemosensors to Cd^{2+} ions is interfered by Zn^{2+} ions, since both the metal ions possess similar properties.[10,11] Hence, there is a need for developing newer Cd^{2+} chemosensors, which are cheap and easily available.

Quinoline- and piperazine- based Cd^{2+} sensors have been earlier reported.[12-14] However, quinoline-linked piperazines as Cd^{2+} chemosensors are very scarce in the literature.[15] These fluorophores emerge as selective chemosensors for Cd^{2+} ions, although the field of chemosensing has several reports on molecules with various functionalities acting as selectors of various metal ions. More studies on quinoline- based and piperazine-based Cd^{2+} sensors would develop lead molecular sensors for the metal ions.

β-cyclodextrin (β-CD, cyclic oligosaccharides containing seven α-D-glucopyranose units) is a tapered doughnut- shaped, non-toxic molecule.[16] This molecule has a hydrophilic outer surface due to the hydroxyl groups and a hydrophilic cavity due to the etheral oxygens. The cavity can accommodate molecules of appropriate size of guests.[17,18] The complete formation of chemosensors with β-CD can modulate their metal ion sensing property. The understanding of the structure of the host-guest complex can better reveal the metal ion chelating atoms/groups of the guest molecule (chemosensors).[19,20] In this work, we report the Cd^{2+} ion sensing of a quinoline–piperazine conjugate and the effect of β-CD complex formation on the metal ion sensing.

Experimental

All chemicals (AR) were purchased from Aldrich and were used without further purification. UV–visible spectra were recorded on a Jasco V630 spectrophotometer, with 1 cm path length cuvettes. The fluorescence spectra were recorded on a Jasco FP-8300 spectrofluorometer. 2-Dimensional rotating frame Overhouser spectrum (ROESY) was recorded on a Bruker Avance III spectrophotometer operating at 400 MHz in DMSO-d6 under spin lock condition, with a mixing time of 200 ms.

The binding titrations were carried out by preparing stock solutions of the ligand (L) in methanol (1×10^{-3} mol dm^{-3}), and that of β-CD in triply distilled water. Test solutions were prepared by appropriate dilution of the stock solutions to obtain test solutions of concentration 1×10^{-5} mol dm^{-3}. The spectra and the plots corresponding to the binding titrations were drawn using Origin software (ver. 8.0). The test solutions were prepared just before the recording of spectra and they were shaken well before measurements. The temperature of analytical measurements was 25±3 °C.

Results and discussion

The ligand **L** showed two absorption bands at 252 nm and 323 nm respectively (Fig. 1(a)) which correspond to the π→π* (253 nm) and n→π*

(323 nm) transition. β-CD solution was added to **L** in aliquots, keeping the concentration of the latter fixed. The increasing amount of β-CD led to a hyperchromic shift of absorption, indicating that the ligand L most likely formed a complex with β-CD. The fluorescence spectral titration of the **L**–β-CD binding was carried out in a similar way discussed above. The fluorescence spectral changes were more pronounced than the changes in absorption as shown in Fig. 1(b). The fluorescence of **L** was enhanced on the stepwise increase of the concentration of β-CD, without appreciable shift of the wavelength of emission. This enhancement of fluorescence is attributed to the inclusion complex formation of **L** with β-CD.[21,22] In order to determine the stoichiometry and binding constant of the **L**–β-CD complex, the double reciprocal Benesi-Hildebrand plot[23] (Supplementary data, Fig. S1) was plotted following the equation,

$$\frac{1}{I - I_0} = \frac{1}{I'} + \frac{1}{(I' - I_0)K[\beta - CD]}$$

where I_0, I, and I' are the fluorescence intensities of **L** in water, in β-CD of various concentrations, and at the maximum concentration of β-CD, respectively. The determined binding constant (K) value was 1213.83 mol^{-1} dm^3. The linearity of the plot suggests a 1:1 stoichiometry the **L**-β-CD complex.

To study the mode of binding of the guest (**L**) and the host (β-CD) molecules, we recorded 2D ROESY spectrum of the complex (Fig. 2(a)). The ROESY

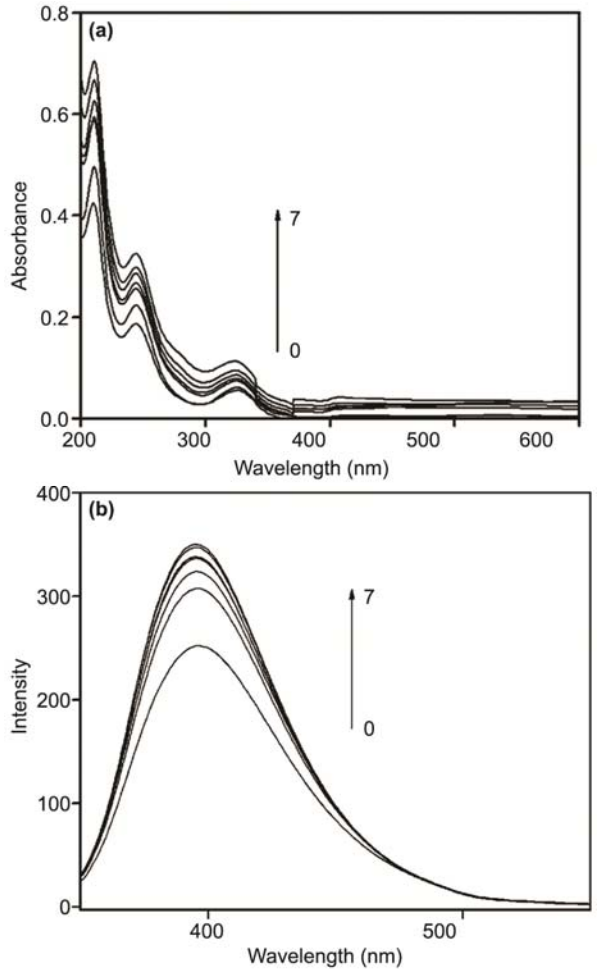

Fig 1 – (a) Absorbance spectra of L at various added amounts of β–CD. The numbers on the arrow indicate the change in the absorbance on increasing concentration of β-CD. (b) Fluorescence spectra of L at various added amounts of β–CD. The numbers on the arrow indicate the change in the intensity of fluorescence on increasing concentration of β-CD.

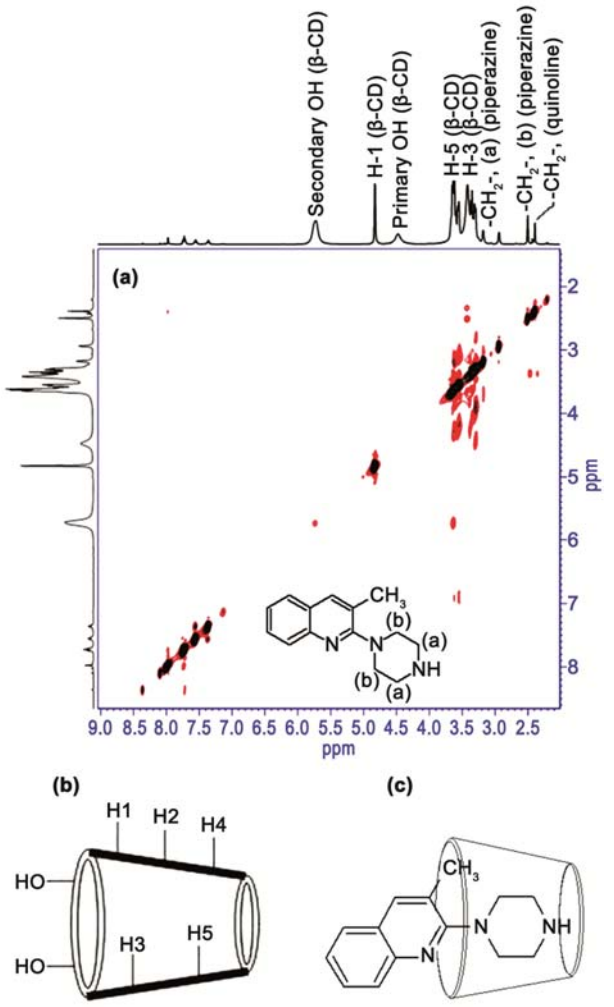

Fig 2 – (a) 2D ROESY spectrum of L–β-CD complex showing interaction between protons of the host and the guest molecules. (b) Schematic representation of β-CD. (c) Schematic representation showing the mode of binding in the L–β-CD complex.

spectrum provided information about the proximity of the protons of the β-CD and the **L** molecules. The inner rim of the β-CD molecule is lined with H–5 and H–3 protons of the gluopyranose rings (Fig. 2(b)). The signals at around 3.6 ppm are due to H-5 and at 3.3 ppm are due to H-3 protons. The $–CH_2–$ protons of the piperazine moiety of **L** resonated at 2.552 and 3.215 ppm (designated as (a) and (b) protons) and the methyl substituent on quinoline ring showed a signal at 2.385 ppm. The $–CH_2–$ (b) protons of piperazine and the $–CH_3$ protons on quinoline showed cross peak with the H-5 proton signal of β-CD. Similarly, the protons of piperazine showed signal which cross-correlated with the signal contour of H-3 proton of β-CD. This indicates that the β-CD molecule encapsulated ligand **L** as shown schematically in Fig. 2(c) (The aromatic protons of **L** do not show cross peaks with β-CD protons).

The ligand **L** was studied for its metal-ion sensing behavior by carrying out a titration of various metal ions against **L** (concentration of **L** and the metal ions being 1×10^{-5} mol dm^{-3}). The metal ion selectivity was studied using UV-visible absorption and fluorescence spectroscopy following either enhancement or diminishing of the absorption and fluorescence spectral bands (Fig. 3). The absorption spectrum of **L** showed hypochromic shifts on the addition of any of the metal among the pool of metal ions, viz., Na^+, Ca^{2+}, Ba^{2+}, Mg^{2+}, Pb^{2+}, Mn^{2+}, Fe^{2+}, Ni^{2+}, Cu^{2+}, Cd^{2+}, Ti^{2+}, Zn^{2+}, Vo^{2+}, Cr^{3+}, and Al^{3+} (Fig. 3(a)). However, there is no significant change between the absorption of metal ion-added **L** and that of free **L**. Figure 3(b) shows the fluorescence spectral titration of the metal ion-**L** interaction. Most of the metal ions exhibit quenching of fluorescence of **L**. However, addition of Cd^{2+} enhanced the fluorescence, revealing the

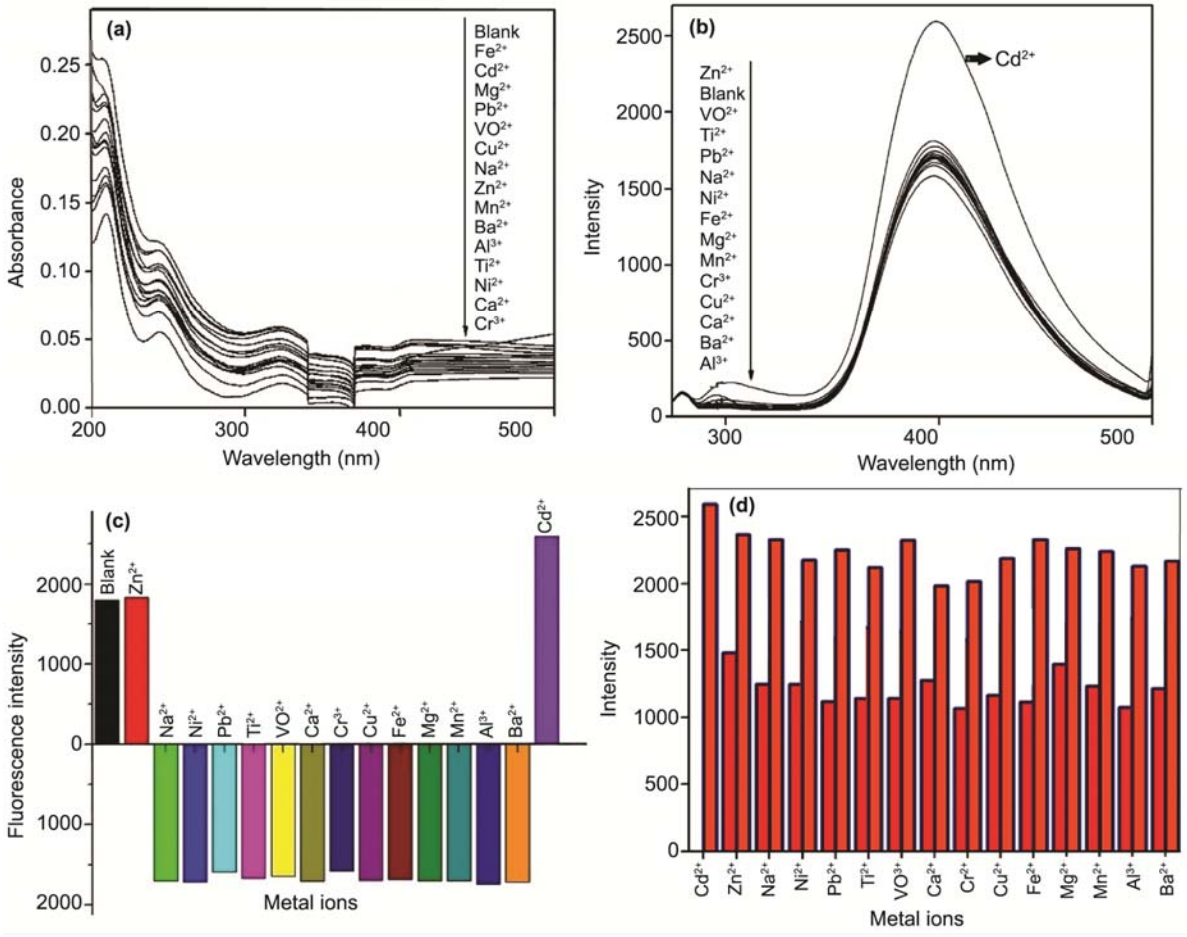

Fig 3 – (a) Absorption spectra of various metal ion added L in aqueous medium. (b) Fluorescence spectra of L with various added metal ions in aqeous medium. Addition of Cd^{2+} ion results in an enhancement of fluorescence. (c) Intensity differences in the fluorescence of metal ion–added L in aqueous medium. (d) Fluorescence intensities showing the competitive binding of Cd^{2+} to L in presence of other metal ions.

selective binding of Cd^{2+} by **L**. This enabled the fluorescence chemosensing of Cd^{2+} by **L**. The fluorescence intensity changes are clearly shown in Fig. 3(c).

A competitive binding experiment was carried out to know the possible influence of other metal ions on the **L**-Cd^{2+} binding. The ligand and each of the metal ions were mixed and Cd^{2+} was then added to the mixture. Addition of Cd^{2+} enhanced the fluorescence in each case, revealing that in the presence of each of the studied other metal, Cd^{2+} binds competitively. Figure 3(d) shows a comparison of intensity of the various metal ion added **L**-Cd^{2+} solutions, indicating the Cd^{2+} ion selectively of **L**.

The stoichiometry of the **L**-Cd^{2+} complex was determined from the Job's plot (Supplementary data, Fig. S2(a)). The fluorescence enhancement of **L** by Cd^{2+} was attributed to the 1:1 complex formation between Cd^{2+} and **L**. The association constant of the complex was calculated from the Benesi-Hildebrand plot shown in Fig. S2(b) as 3044 mol^{-1} dm^3.

The limit of detection of Cd^{2+} by **L** was also determined. From the linear plot of concentration of Cd^{2+} versus the relative intensity of fluorescence (Supplementary data, Fig. S2(c)), the limit of detection was determined as $LOD = KS_b/m$ (where S_b and m are the standard deviation of the blank measures and the calibration sensitivity respectively, and K = 3 for the method detection limit).[24,25] The calculated detection limit value was found to be 1.908×10^{-7} mol dm^{-3}.

The metal-ion selectivity of **L** was studied in the presence of β-CD, to understand the influence of the host molecule on the chelating effect of **L**. To an equimolar solution of **L**-β-CD (1×10^{-5} mol dm^{-3}), various metal ions were added. However, no significant difference in the fluorescence response of the host guest complex was observed on addition of any of the metal ions. Cd^{2+} also did not lead to an enhancement of fluorescence, instead a weak quenching was observed. Hence, it was inferred that the β-CD molecule blocked the metal ion binding site of **L**. The encapsulation of fluorescent chemosensors by β-CD has notably worked well for the sensing of Zn^{2+} and Ca^{2+} ions.[19,20] In these cases also the sensing was based on fluorescence enhancement on the binding of the metal ions for which the chemosensor showed selectivity. Fluorescence enhancement based sensing of Cd^{2+} in the presence of β-CD is reported herein. In all cases, it is obvious that the chelating moiety stands outside the host molecule. Hence, the extent of modulation of the sensing depends on the mode of binding of the guest molecule with β-CD.

From the above discussion, it is obvious that 3-methyl-2-(piperazin-l-yl)quinoline forms a 1:1 host-guest complex with β-CD. The binding constant is 1213.83 mol^{-1} dm^3. The compound acts as a chemosensor for Cd^{2+} ions in aqueous medium based on its fluorescence response through enhancement. The stoichiometry of the Ligand–Cd^{2+} complex is 1:1 and the association constant is 3044 mol^{-1} dm^3. The lower limit of detection of Cd^{2+} by the ligand is 1.908×10^{-7}. When β-CD encapsulates the molecule, the ion binding site is blocked and hence piperazinylquinoline does not effectively bind metal ions and senses Cd^{2+} in aqueous β-CD solution. This work provides indirect information on the moiety of the molecule which is responsible for the fluorescence enhancement-based detection of Cd^{2+}. The present chemosensor works well for Cd^{2+} ion sensing and does not respond to Zn^{2+} ion, even though both the metal ions have similar chemical properties.

Supplementary data

Supplementary data associated with this article are available in the electronic form at http://www.niscair.res.in/jinfo/ijca/IJCA_57A(02)163-167_SupplData.pdf.

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