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# Turn on fluorescence strip based sensor for recognition of $Sr^{2+}$ and CN<sup>-</sup> via lowerrim substituted calix[4]arene and its computational investigation



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## ABSTRACT

Fluorescence sensor L designed around a calix[4]arene scaffold, bearing two fluorogenic aminoquinoline moities, has been synthesized. It is found to be selective and sensitive towards  $Sr^{2+}$  and  $CN^-$  over a wide range of cations and anions in a spectrofluorometric study in acetonitrile. The ion-binding property of L was monitored by fluorescence spectroscopy, UV-vis spectroscopy, ESI-MS, <sup>1</sup>H NMR, FT-IR investigation and PXRD study. The host L shows a minimum detection limit which is 1.36 nM for Sr<sup>2+</sup> and 1.23 nM for CN<sup>-</sup> having concentration range 5–120 nM and 5–115 nM respectively. The calculated binding constants for L:Sr<sup>2+</sup> and L: CN<sup>-</sup> are respectively  $8.859 \times 10^8$  M<sup>-1</sup> and  $8.574 \times 10^8$  M<sup>-1</sup>. Our host L has been utilised in formation of a user-friendly, affordable, and disposable paper-based analytical device (PAD) for rapid chemical screening of  $Sr^{2+}$  and  $CN^{-}$  ion via single strip. Moreover, the optimization of probe L has also been done by the MOPAC-2016 software package using NM7 popular method resulting -21.71 kcals/mol heat of formation and also determined the HOMO-LUMO energy band gap for L L:Sr<sup>2+</sup> and L: CN<sup>-</sup>. Further, molecular docking score has been calculated using HEX software. The applicability of our probe in real samples containing  $Sr^{2+}$  and  $CN^{-}$  has also been checked by emission study with 94–99% recovery.

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## 1. Introduction

Detection of cations, anions and neutral molecules is currently stint of major consideration in the modern research work due to their prevalent applications in chemical, biological and environmental assays. Though  $Sr^{2+}$  is broadly used in optical industry, painting industry and military industry, it is considered as a major component of 'dirty bomb'. Besides, the Department of Energy entails a field instrument that can contrivance the real-time characterization and observation of radioactive Sr-90 inside high level waste tanks [1-2]. Despite of acute toxicity, CN<sup>-</sup> is used in many industries such as synthetic fibres and resins, herbicides, gold extraction, etc. and also can be found in many fruits and plants. Consequently, any fortuitous release of the extremely toxic cyanide certainly leads to water and environmental corruptions [3-6]. The homeland security and antiterrorist activities with the help of Sr<sup>2+</sup> and harmfulness of CN<sup>-</sup> have elicited substantial attentiveness in developing a convenient and easy-to-use molecular sensor.

There is a wide range of instrumental techniques for the trace identification of molecular ions but the real-time use of these techniques is

Corresponding author. E-mail address: pinkeshsutariya@gmail.com (P.G. Sutariya). limited due to their expensive instrumentation, not easy to operate them on-site and lack of portability. Simultaneously, one tactic which draws the attention of researchers is fluorometry technique. The interest has been directed towards the making of simple  $\pi$ -electron-rich molecule as a fluorescence sensors. In fluorescence-based sensing method. fluorophore is tethered with an ionophore to build fluoroionophore in order to detect molecular guest ions. The ionophore acts as a binding site for the analyte whereas the fluorophore serves as a signalling unit which provides optical response after detection of a recognition event. It has emerged as one of the most robust method due to its high efficiency, simplicity and ultra-sensitivity to construct an effective and economic chemosensor.

Calixarenes [7–8], produced by the condensation of p-substituted phenols with aldehydes, a part of macrocyclic family, paves new avenues in diverse areas. The popularity of calixarenes, especially calix[4]arene, arises owing to their amphiphilic nature, existence of platform for appropriate substitution at lower and upper-rim, presence of arene core and flexible arms to provide suitable and selective coordination environment. To broaden the area of sensing molecular ions, the architecture of functionalized calix[4]arene [9-11] and fluorometry technique are used. Different motifs are appended at the upper rim as well as lower rim of calix[4]arene which act as tweezers and chelate the guest ions. Due to this, the efficiency of chemosensor is increased which can enable researchers to detect a wide range of chemicals with high sensitivity and fast response time using various mechanisms [12–19].

As the unique topology of calix[4]arenes offer a wide range of scaffolds for making of platforms for sensors, a myriad study in molecular recognition have been achieved and numerous endeavours have been devoted by our group [20–23]. In an ensuing study, by introducing a new fluorescence probe (L) (Scheme 1), we have tried to exploit a new approach to prepare a selective fluorescence probe for  $Sr^{2+}$  and  $CN^-$ . We have also completed a very challenging task that is on-spot monitoring of recognized ions in real samples as well as computational monitoring. A single step "dip-and-read" based method is also developed by using the fluorescent indicator and qualitative strategy.

## 2. Experimental

2.1. Synthesis of compound (A-E) and its characterization [Scheme 1, Figs. S1–S2 are described in ESI<sup>+</sup>

### 2.1.1. General procedure for spectroscopic study

As acetonitrile is miscible with water, we have prepared stock solutions of analytes such as perchlorate salts of metal ions  $M^+$  (Li<sup>+</sup>, Ag<sup>+</sup>, Na<sup>+</sup>, K<sup>+</sup>),  $M^{2+}$  (Zn<sup>2+</sup>, Ca<sup>2+</sup>, Cd<sup>2+</sup>, Fe<sup>2+</sup>, Ba<sup>2+</sup>, Co<sup>2+</sup>, Hg<sup>2+</sup>, Cu<sup>2+</sup>, Ni<sup>2+</sup>, Mn<sup>2+</sup>, Pb<sup>2+</sup> and Sr<sup>2+</sup>),  $M^{3+}$  (Fe<sup>3+</sup>, La<sup>3+</sup>, As<sup>3+</sup>, Nd<sup>3+</sup>, Ce<sup>3+</sup>, Cr<sup>3+</sup>),  $M^{4+}$  (Zr<sup>4+</sup>) and tetrabutyl ammonium (TBA) salts of anions (F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, NO<sub>3</sub><sup>-</sup>, HSO<sub>4</sub><sup>-</sup>, CN<sup>-</sup>, H<sub>2</sub>PO<sub>4</sub><sup>-</sup>, S<sup>2-</sup> and CH<sub>3</sub>COO<sup>-</sup>) in acetonitrile with the concentration of  $1 \times 10^{-6}$  M. Simultaneously, the stock solution of ligand L was also made in acetonitrile with the concentration of  $1 \times 10^{-8}$  M. Then the stock solutions were diluted to desired concentration when needed. The spectroscopic properties of L were examined in mixed aqueous organic medium [acetonitrile/4-(2-

## 2.2. Spectroscopic extents

Absorption and emission spectra of the novel synthesized probe L were recorded by making solution as above mentioned in Section 2.1.1. The compound shows the absorption peak in the region between 210 and 500 nm, wherein the peak at 284 nm indicates  $\pi$ -  $\pi$ \* transition of 4-aminoquinoline system. The ligand exhibits a strong emission peak at 575 nm with excitation at the absorption maxima of the 4-aminoquinoline moiety that is at 284 nm.

## 2.3. Preparation of real sample assay

The tap water was taken directly for the analysis without doing purification. The lake water collected from the local lake (Gomati Lake, Dakor) was first filtered through nylon microporous filter to remove unnecessary suspension. The industrial waste water samples (100 ml) were collected from industrialized sewage (vatava). The water sample was exposed to extraction procedure. Our compound was soluble in chloroform as well as in acetonitrile but as acetonitrile is miscible with water, chloroform was preferred to prepare the solution of the compound. Then in a separating funnel, we procured 60 ml of L (10 nM) solution and 40 ml of water sample and extracted Sr<sup>2+</sup> by shaking for half an hour. Then we separated organic layer and dehydrated organic phase with anhydrous Na<sub>2</sub>SO<sub>4</sub>. The extraction was repetitive done by three to four times. Then different concentrations of cyanide (10 nM, 20 nM, 30 nM, 40 nM, 50 nM and 100 nM) were spiked to the solution. In a similar manner, industrial waste water samples for Sr<sup>2+</sup> were taken for the analysis and above-mentioned procedure was done. Then the fluorescence intensity for each sample was recorded for quantification of developed method.



Scheme 1. Schematic representation showing synthesis pathway of 5, 11, 17, 23-tetra t-butyl- 26, 28 dimethoxy 25, 27 amidoquinoline calix[4]arene (L).

## 2.4. Construction of paper-based device

The outline and photograph of a single paper-based analytical device (PAD) for Sr<sup>2+</sup> and CN<sup>-</sup> detection are shown in [Fig. S3 (ESI<sup>†</sup>)]. It works in the principle of capillary flow mechanism in paper. We have performed simple fabrication technique to create the specific patterned layouts of single or multi well patterns onto the nitrocellulose membrane (NCM). The fabrication is performed mainly three components i.e. backing card, NCM, punched NCM. Initially, the desired control (C) hole, test hole (T1 and T2) was created in NCM using punch tool. Furthermore, backing card is being used to stick plain NCM on it. Then, on NCM stacked backing card, punched NCM were uniformly stacked to perform to capillary flow of sample solution. This fabricated PAD is used for detection of  $Sr^{2+}$  and  $CN^{-}$  ion as test strip as shown in [Fig. S3 (ESI<sup>†</sup>)]. The detection was typically performed as following: for single ion detection: 5 µL of the L sample was immobilized into NCM and kept it for 15 min for drying. And then, dip in 5 ml of solution of Sr<sup>2+</sup> and CN<sup>-</sup> ion at different concentration was added. After the solution totally soaked in 5 min, the test results could be read by naked eve under UV light (365 nm) illumination, and the corresponding fluorescent images were captured directly by a VIVO digital camera. Similar method is performed for the detection of dual ion in single test strip.

### 3. Results and discussion

#### 3.1. Fluorescence interaction studies of L

In this feature work, we have employed aminoquinoline [24] motif as a fluorophore with calix[4]arene for the detection of molecular ions. To fully harness the binding abilities of fluorescent probe L, the fluorescence spectral investigation was performed in acetonitrile produced by addition of several perchlorate salts of metal ions and tetrabutyl ammonium salts of anions mentioned in Fig. 1. It shows that out of a large number of metal ions and anions, L performs with high selectivity to  $Sr^{2+}$  and  $CN^{-}$  by enhancing fluorescence intensity compared to the original spectra of L. We have kept equal concentration  $(1 \times 10^{-8} \text{ M})$  for L, various aforesaid perchlorate salts and tetrabutyl ammonium salts as mentioned above in acetonitrile. The overall emission changes were dramatic: 1.76 fold for Sr<sup>2+</sup> and 1.89 fold CN<sup>-</sup> with L [Fig. 1 A and B]. Two aminoquinoline groups are linked to calix[4] arene in such a way that carbonyl groups of the fluorophore interacts with Sr<sup>2+</sup> and –NH linkage participates in the complexation process with CN<sup>-</sup>. Consequently, this binding results in enhancement of fluorescence intensity which is introduced by Chelation Enhanced Fluorescence (CHEF) mechanism. The reason behind CHEF process is that the binding of Sr<sup>2+</sup> to ligand L reduces the electron-donating ability of N and O to aromatic rings, causing a remarkable increment in the emission intensity. Moreover, our probe has coordination site having N. O and – CONH linkage as a binding site which can detect hard acid  $Sr^{2+}$  easily. Additionally, CN<sup>-</sup> interacts with –CONH linkage via hydrogen bonding which leads to the enhancement of fluorescence intensity. Therefore, it is predicted that Sr<sup>2+</sup> and CN<sup>-</sup> closely interact with L and cause obvious change in fluorescence intensities with respect to other large number of cations and anions. Hence, for guantitative analysis we have selected these two ions (Sr<sup>2+</sup> and CN<sup>-</sup>) for further examination.

## 3.2. Sensing properties of probe L

In order to acquire swift and sensitive analysis of our fluoroionophore, we added  $1 \times 10^{-6}$  M solutions of Sr<sup>2+</sup> and CN<sup>-</sup> into  $1 \times 10^{-8}$  M solution



**Fig. 1.** (A-D). (A-B) Fluorescence spectral changes of L ( $1 \times 10^{-8}$  M) caused by binding with different cations (from top to bottom,  $Zn^{2+}$ ,  $Fe^{3+}$ ,  $Fe^{3+}$ ,  $Mn^{2+}$ ,  $La^{3+}$ ,  $Ad^{3+}$ ,  $As^{3+}$ ,  $Cd^{2+}$ ,  $Pr^{3+}$ ,  $Zt^{4+}$ ,  $Ag^+$ ,  $Ba^{2+}$ ,  $Co^{2+}$ ,  $Ca^{2+}$ ,  $Ce^{3+}$ ,  $Li^+$ ,  $Hg^{2+}$ ,  $Na^+$ ,  $K^+$ ,  $Ni^{2+}$ ,  $Pb^{2+}$ , and  $Cu^{2+}$ ) and anions (from top to bottom,  $F^-$ ,  $Cl^-$ ,  $Br^-$ ,  $I^-$ ,  $HsO_4^-$ ,  $H_2PO_4^-$ ,  $NO_3^-$ ,  $S^{2-}$  and  $CH_3COO^-$ ). (C-D) Fluorescence spectral traces obtained during the titration of L ( $1 \times 10^{-8}$  M) with increasing concentration 5–120 nM and 5–115 nM of Sr<sup>2+</sup> and CN<sup>-</sup> respectively at pH 7.

to the fluoroionophore (L). Fluorescence titration has explored by gradually varying the concentration of  $Sr^{2+}$  (5–120 nM) and  $CN^-$  (5–115 nM) and keeping the concentration of L constant because sensitivity is crucial part for any sensor [Fig. 1 (C-D)]. The calibration curve shows good linearity with correlation coefficient of 0.9922 for  $Sr^{2+}$  and 0.9904 for  $CN^-$  [Fig. S4 (A-B) (ESI†)]. The limit of detection (LOD) and the limit of quantification (LOQ) were calculated by the minimum level at which the solution of  $Sr^{2+}$  and  $CN^-$  can be readily quantified with accuracy. LOD and LOQ were calculated according to the 3.3  $\sigma$ /s and 10  $\sigma$ /s criteria respectively where " $\sigma$ " is the standard deviation of intercept of regression equation and "s" is the slope of the corresponding calibration curve. The LOD was found to be 1.36 nM for  $Sr^{2+}$  and 1.23 nM for  $CN^-$ . The limit of quantification (LOQ) has also been calculated for L and was found to be 4.52 nM for  $Sr^{2+}$  and 3.74 nM for  $CN^-$ .

### 3.3. Determination of association constants

Association constants for fluoroionophore were calculated by using fluorescence titration data following the previously reported articles [25]. Here, we have displayed representative spectra showing the changes observed in emission intensities upon the addition of increasing concentration of ions. According to this procedure, the fluorescence intensity (F) scales with the metal ion/anion concentration ([M]) through (F<sub>0</sub>—F)/(F-Fœ) = ([M]/K<sub>diss</sub>)<sub>n</sub>. The binding constant (Ks) is obtained by plotting Log[(F<sub>0</sub>—F)/(F-Fœ)] vs Log[M], where F<sub>0</sub> and Fœ are the relative fluorescence intensities without addition of guest metal ions and with maximum concentration of metal ions (when no further change in emission intensity takes place), respectively. The value of Log [M] at Log[(F<sub>0</sub>—F)/(F-Fœ)] = 0 gives the value of log (K<sub>diss</sub>), the reciprocal of which is the binding constant (Ks). The observed binding constant from fluorescence spectra for Sr<sup>2+</sup> and CN<sup>-</sup> are respectively 8.859 × 10<sup>8</sup> M<sup>-1</sup> and 8.574 × 10<sup>8</sup> M<sup>-1</sup>[Fig. 2(A-B)].

# 3.4. Quantum yield calculation of L with $Sr^{2+}$ and $CN^{-}$

The quantum yield was calculated by following equation

 $\varphi = \varphi \text{std} \frac{(F \times \text{Astd} \times \eta)}{(F\text{std} \times \text{A} \times \eta\text{std})}$ 

where F and Fstd are the areas under the fluorescence emission curves of the  $\rm Sr^{2+}$  and  $\rm CN^-$  ions complexes with L and only standard L

respectively. A and Astd are the areas under relative absorbance of the Sr<sup>2+</sup> and CN<sup>-</sup> ions complexes with L and standard L at the excitation wavelength, respectively.  $\eta$  and  $\eta_{std}$  are the refractive indices of solvent (acetonitrile) used for the Sr<sup>2+</sup>, CN<sup>-</sup> and standard (L), respectively. The Sr<sup>2+</sup>, CN<sup>-</sup> and the standard (L) were excited at the same wavelength. The quantum yield of fluoroionophore L was obtained using emission spectra of standard fluorophore (4-aminoquinoline). The reported quantum yield of 4-aminoquinoline [26] was approximately 0.23 and that of L with Sr<sup>2+</sup> and CN<sup>-</sup> ion complex were found to be 0.41 and 0.45 respectively. Thus, when Sr<sup>2+</sup> and CN<sup>-</sup> were attached to L, the quantum yield increases. Hence L provides a sensitive means to recognize Sr<sup>2+</sup> and CN<sup>-</sup> by direct fluorescence measurement.

## 3.5. UV-visible spectral observations of L

To examine the chromogenic behaviour and selectivity of L, UVvisible titration experiment was carried out for  $Sr^{2+}$  and  $CN^-$ . The original absorbance band of ligand L was at 284 nm. It is noteworthy that when we added 5 nM of  $Sr^{2+}$  and  $CN^-$  solutions, it shifted affectedly and a new band rises at 315 nm and 293 nm respectively which indicates bathochromic effect or blue shift as displayed in [Fig. 3(A-B)]. The interaction of  $CN^-$  with amide linkage of L by forming hydrogen bonding and  $Sr^{2+}$  binding with ketonic group via electrostatic interaction of scaffolds are the causes of blue shift. To know the detection limit of L towards  $Sr^{2+}$ and  $CN^-$ , we have also performed UV-vis titration by varying concentration of selective ions (0 nM- 100 nM) [Fig. 3(C-D)]. From this exploration, if we compare both techniques- fluorescence and UV-vis experiment, we can state that fluorescence technique is more unswerving than absorption study in terms of sensitivity and low detection limit.

### 3.6. Determination of complex stoichiometry

To determine the stoichiometric ratio of L with  $Sr^{2+}$  and  $CN^-$ , we have implemented different studies like ESI-MS, job's plot method, FT-IR and powder XRD investigation. The formation of 1:1 complex was confirmed by ESI-MS, where the spectrum shows molecular ion peak m/z at 1047.8 whereas in the presence of  $Sr^{2+}$  show peak at 1136.4 [Fig. S5 (ESI†)]. Further in this direction, the stoichiometry of the complex formed (1: 1) has also been derived based on the Job's plot by performing UV–visible experiment [Figs. S6-S7 (ESI†)]. After the confirmation of 1:1 complex formation ratio, we have also recorded FT-IR spectra of pure ligand L, L+  $Sr^{2+}$  by potassium bromide (KBr) disk



Fig. 2. (A-B). Association constant diagram for (A) Sr<sup>2+</sup> and (B) CN<sup>-</sup> with L ligand from fluorescence titration experiment.



**Fig. 3.** (A-B) UV-visible absorption spectral changes of L ( $1 \times 10^{-6}$  M) caused by binding with Sr<sup>2+</sup> and CN<sup>-</sup>, (C-D) The UV-visible spectra of L ( $1 \times 10^{-6}$  M) after adding different concentration of Sr<sup>2+</sup> and CN<sup>-</sup> (0, 10 nM, 0.100 nM) respectively.

method and scanned at the wave number region 4000–600 cm<sup>-1</sup>. Moreover, FT-IR comparative experiment was also executed in which the binding of Sr<sup>2+</sup> with ligand L was evaluated. The broadening of – CH aromatic stretching peak, change in –C=O (ketone) peak in presence of Sr<sup>2+</sup> will give assurance of effective binding of Sr<sup>2+</sup> with L via electrostatic interaction. [Fig. S8 (ESI†)]. Besides, for more confirmation of binding L: Sr<sup>2+</sup>, the PXRD study has also been conducted. In the Fig. 4, the powder diffraction patterns of the ligand L (C<sub>68</sub>H<sub>78</sub>O<sub>6</sub>N<sub>4</sub>) and L: Sr<sup>2+</sup> (C<sub>68</sub>H<sub>78</sub>O<sub>6</sub>N<sub>4</sub>Sr<sup>2+</sup>) are presented. The experimental 20 range is 5.00 to 80.00° with a step size of 0.01° and a counting time of 60s per step. The PXRD patterns of L and L: Sr<sup>2+</sup> exhibited intense peaks at 20 values

19.05° (21–2) and 38.63° (102) respectively as depicted in Fig. 4. From the overly of PXRD patterns of metal complex, new peaks and peak shift were observed which give reassurance of L:  $Sr^{2+}$  binding. Table S1 reveals that ligand L and  $Sr^{2+}$  has monoclinic crystal system with space group P2/m. Analytical indexing of the powder patterns for ligand L and L with  $Sr^{2+}$  are summarized in Table S2 and Table S3 respectively.

## 3.7. Recognition of CN<sup>-</sup> with L via hydrogen binding

The complexion mechanism between L and  $CN^-$  was investigated by <sup>1</sup>H NMR titration study in DMSO-*d*<sub>6</sub>. Different amounts of  $CN^-$  was added



Fig. 4. The plot shows results of PXRD investigation of the ligand L and L with Sr<sup>2+</sup>.

to a solution of L in DMSO-*d*<sub>6</sub> and then the spectrum was recorded. Upon addition of 10-fold excess CN<sup>-</sup> into L ligand, the –NH peak at  $\delta$  = 8.71 ppm disappears because of the hydrogen bonding with –NH group of amide linkage of ligand L [Fig. S9 (ESI<sup>+</sup>)]. The fading of –NH peak will give assurance of binding of CN<sup>-</sup> ion with amide linkage of L.

## 3.8. pH evaluation of L

It is indispensable to check at which pH our fluorescence probe works effectively. The effect of pH on fluorescence spectrum L in the presence and absence of  $Sr^{2+}$  and  $CN^-$  was studied by measuring fluorescence intensity of L at different pH values. It was observed that the interaction of L with  $Sr^{2+}$  and  $CN^-$  was the most effective at pH 7 as shown in [Fig. S10 (A-B) (ESI<sup>†</sup>)] by exhibiting maximum enhancement which indicates that our chemosensor will act efficiently in neutral condition.

### 3.9. Interference study

As in real samples, various other metal ions and anions are also present along with the  $Sr^{2+}$  and  $CN^-$  and can affect the sensing process, it is necessary to investigate functional properties and selective nature of L towards  $Sr^{2+}$  and  $CN^-$  in the presence of co-existing cations and anions. This interference study was carried out using 10 equivalents of other cations with  $Sr^{2+}$  separately. In a same way, 10 equivalents of different anions were taken with  $CN^-$  to check whether it affects the fluorescence intensity or not. The results of this experiment lead us to note that no other competitive ions displayed any significant interference. The fluorescence intensity of L:  $Sr^{2+}$  and L:  $CN^-$  did not change drastically upon addition of aforementioned cations and anions as depicted in [Fig. 5(A-B)]. Plausible binding mechanism through hydrogen bonding and electro static interaction with L ligand by  $Sr^{2+}$  and  $CN^-$  is shown in Fig. 6.

## 3.10. Application of the method to real sample assay

After studying the sensing properties of our fluorescence probe L with various molecular ions, we have also investigated its properties in real sample assays such as different industrial waste water samples towards  $\rm Sr^{2+}$  and  $\rm CN^-$  by using fluorescence titration. The standard

addition method was applied to evaluate the validity of the proposed sensor. Table S4 and Table S5 demonstrate analytical results of them with excellent recovery of spiked  $\text{Sr}^{2+}$  and  $\text{CN}^-$  ranged from 94 to 99%, proving the validity of the developed technique. We have also carried out selectivity factor calculation in presence of different ions with L +  $\text{Sr}^{2+}$  (10 nM) and L +  $\text{CN}^-$  (10 nM) at pH 7 (Table S6 and S7, ESI). The proposed technique is compared with reported methods for determination of  $\text{Sr}^{2+}$  and  $\text{CN}^-$  (Table S8). This comparison undoubtedly endorses that proposed fluorometric method is superior to others in terms of sensitivity, selectivity and binding ability to recognize  $\text{Sr}^{2+}$  and  $\text{CN}^-$  [27–31].

## 3.11. Outcomes of paper based analytical device (PAD)

Fluorometric probes for dual ion detection are commonly used in cuvette-based tests employing conventional spectrometers. This approach is inconvenient and cannot be used for on-site detection. To overcome this problem, we have developed a paper-based analytical device (PAD) which is based on fluorescent calix[4]arene (L) immobilized on PAD as sensing probes contained within NCM membrane as illustrated in Fig. 7. NCM was selected as substrate due to its superior ability to wick aqueous or organic solutions by capillary action, among other recognized qualities that make pumps or high-power source requirements not necessary. The sensing mechanism observed here is based on chelation enhanced fluorescence effect where the fluorescence enhancement of probe L occurs simultaneously due to its distinctive interaction of designed calix[4]arene for cations and anions. Fig. 7 elucidates the fluorescent calix[4]arene (L) based probe which is immobilized on PAD and can produce blue fluorescent colour under UV light. Thus, to aid the determination of fluorescent changes with portable, handheld and test strip reader, we have tried to prepare a simple dip test strip-based assay which can detect  $Sr^{2+}$  and  $CN^{-}$  ions in neat and low molar concentration aqueous solution. A drop of L solution was placed at delineated area test hole (T1 and T2) along with control, dried at 37 °C, and a fluorescent change was measured. As shown in [Fig. 11(A) (ESI<sup>†</sup>)] after the addition of different concentration of  $Sr^{2+}$  ranging from  $10^{-6}$  to  $10^{-3}$  M, excitedstate photons from the calix[4]arene are transferred to the analyte displaying a proficient enhancement in presence of  $Sr^{2+}$ . Likewise,



**Fig. 5.** (A-B). (A) The histogram shows relative changes in fluorescence intensity of L ( $1 \times 10^{-8}$  M) with Sr<sup>2+</sup> in presence of other cations (a = Ligand + Sr<sup>2+</sup>, b = a + Za<sup>2+</sup>, c = a + La<sup>3+</sup>, d = a + Mn<sup>2+</sup>, e = a + Cd<sup>2+</sup>, f = a + Ba<sup>2+</sup>, g = a + Co<sup>2+</sup>, h = a + Ni<sup>2+</sup>, i = a + Zt<sup>4+</sup>, j = a + Ca<sup>2+</sup>, k = a + Ce<sup>3+</sup>, l = a + Li<sup>+</sup>, m = a + Ag<sup>+</sup>, n = a + Fe<sup>2+</sup>, o = a + Fe<sup>3+</sup> a + Co<sup>2+</sup>, p = a + Hg<sup>2+</sup>, q = a + Na<sup>+</sup>, r = a + K<sup>+</sup>, s = a + Nd<sup>3+</sup>, t = a + Pb<sup>2+</sup>, u = a + Pr<sup>3+</sup>, v = a + Cu<sup>2+</sup> and w = a + As<sup>3+</sup>), (B) The histogram shows relative changes in fluorescence intensity of L ( $1 \times 10^{-8}$  M) with CN<sup>-</sup> in presence of other cations (a = Ligand + CN<sup>-</sup>, b = a + F<sup>-</sup>, c = a + Cl<sup>-</sup>, d = a + Br<sup>-</sup>, e = a + l<sup>-</sup>, f = a + HSO<sup>4</sup>\_4, g = a + H<sub>2</sub>PO<sup>4</sup>\_4, h = a + NO<sup>3</sup>\_4, i = a + S<sup>2-</sup>, j = a + CH<sub>3</sub>COO<sup>-</sup>).



Fig. 6. Plausible binding model of the sensor L, L: Sr<sup>2+</sup> and L: CN<sup>-</sup>.

after the addition of different concentration of  $CN^-$  ranging from  $10^{-7}$  to  $10^{-4}$  M L exhibits a remarkable enhancement depicted in [Fig. S11 (B) (ESI†)]. It can be envisioned by naked eye. These results also indicate that naked eye, this sensor is visibly able to detect ion up to the  $10^{-6}$  M for Sr<sup>2+</sup> ion and  $10^{-7}$  M for CN<sup>-</sup> ion with better sensitivity. It is also significantly less than the recommended Sr<sup>2+</sup> and CN<sup>-</sup> levels mentioned by EPA guidelines. Design for onsite monitoring of Sr<sup>2+</sup> and CN<sup>-</sup> levels using low cost test papers has been shown in Fig. 7.

#### 3.12. Binding nature of L by computational studies

Molecular orbital package (MOPAC) software has used to optimize geometry of ligand L as optimization of the structure is an imperative vision of computational studies [32]. This semi-empirical approach has been executed by applying a Z-matrix of the molecule which was then transformed into its MOPAC input data. Optimization of these data has delivered the specific bond distance, bond angle, dihedral angle of the most stable molecular geometry. The heat formation energy was generated -21.71 kcals/mol using NM7 method. MOPAC calculations produced visual models of the most stable molecular geometry in ball and stick configuration are displayed in [Fig. S12 (ESI†)].

## 3.12.1. HOMO and LUMO analysis

The most important orbitals in a molecule are the frontier molecular orbitals, called highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO). These orbitals determine the way the molecule interacts with other species. The Eigen values of HOMOs ( $\pi$ -donor) and LUMOs ( $\pi$ -acceptor) and their energy gap reflect the chemical activity and the energy gap between them which has been used to prove the bioactivity from keto-enol charge transfer of L. Homo and Lumo orbitals of the L and L with Sr<sup>2+</sup> and CN<sup>-</sup> complexes are plotted in Fig. 8. The charge in HOMO-LUMO energy band gap suggested that the charge transfer of molecules and its explanation of fluorescence enhancement during the recognition event of Sr<sup>2+</sup> and



**Fig. 7.** (A-C). Fluorescent L immobilized dual plasmonic sensor, (A) L containing test strip under fluorescent light (B) Dip in  $Sr^{2+}$  and  $CN^-$  containing sample (C) Read under fluorescent light (365 nm) indicating the presence of  $Sr^{2+}$  (T1) and  $CN^-$ (T2).



Fig. 8. Results of Homo - Lumo orbital analysis of free ligand L,  $L + Sr^{2+}$  and  $L + CN^{-}$  complexes.

CN<sup>-</sup>. The band gap (Fig. 8) reveals that the energy band gap in free ligand L is -0.11363 eV whereas for L-Sr<sup>2+</sup> has shown -0.01193 eV band gap. The band gap of complex L: CN<sup>-</sup> is -0.11308 eV, which supports the enhancement effect in fluorescence intensities of Sr<sup>2+</sup> and CN<sup>-</sup> with L.

#### 3.12.2. Molecular docking investigation

To explore new possibilities of L, we have also carried out molecular docking investigation of our synthesized probe L. For the molecular docking study, we have collected protein structure receptors (*Homo sapiens*) 5ADG, 5VUV, 5VUW, 5UVX, 5VVZ and 5VV1 from protein data bank and calculated energy score of molecular docking by Hex 8.0 software [33]. It was evaluated using molecular dynamics, by their binding affinities, free energy simulations and relative stabilities. The energy values obtained by docking study tabulated in Table S9 and the molecular docking pose of different protein receptors with L is presented in [Fig. S13 (ESI†)], which reveals that the best ligand structure fitting is 5UVW (-471.66 Kcal/mol) compare to other receptors.

### 4. Conclusions

We briefly summarized functionalized calix[4]arene appended with aminoquinoline serving as fluorescence probe for the selective recognition of  $Sr^{2+}$  and  $CN^-$ . The linearity ranges for L:  $Sr^{2+}$  and L:  $CN^-$  are 5–120 nM and 5–115 nM respectively. This technique is also validated by its analytical application in real samples for  $Sr^{2+}$  and  $CN^-$  with 94–99% recovery. Additionally, a label-free dual plasmonic sensor has been developed to selectively determine  $Sr^{2+}$  and  $CN^-$  ions using the fluorescence L. Moreover, PXRD investigation was also performed in order to confirm the binding interaction of cation. In addition to our fluorescence study, we have prepared PAD for on spot monitoring of  $Sr^{2+}$  and  $CN^-$ . The computational investigation has provided assurance of fluorescence enhancement of L with respect to  $Sr^{2+}$  and  $CN^-$ .

#### **Declaration of competing interest**

There are no conflicts to declare.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi. org/10.1016/j.saa.2020.118456.

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