



Coumarin-Picolinothiazone derived Schiff base as fluorescent sensor(OFF-ON) for detection of Al³⁺ ion: Synthesis, Spectral and theoretical studies



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ABSTRACT

New coumarin based Schiff base (**7MIZ**) was synthesized and characterized by various spectral techniques and the true nature was established by X-ray single crystal studies. The probe (**7MIZ**) acted as fluorescent sensor for detection of Al³⁺ ion among different metal ions (chloride salts) with high selectivity. There was a drastic enhancement in the emission intensity at 482 nm showed fluorescence turn 'ON' behavior of the probe when it interacted with Al³⁺ ion which may be due to CHEF (chelation enhanced fluorescence) effect that inhibited the PET (photo-induced electron transfer) mechanism. Further, Job's plot, binding constant value, LOD value, DFT studies established the interaction between probe (**7MIZ**) and Al³⁺ ion and MTT assay studies were carried out for the probe (**7MIZ**) and Al³⁺ ion in Breast cancer cell line (MDA-MB-231).

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1. Introduction

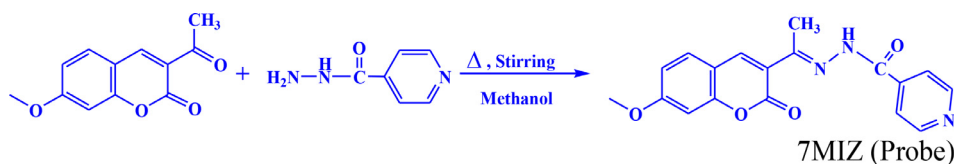
Exploration of highly selective and sensitive fluorescent probes to detect the metal ions have gained attention in recent years due to the vast applications in medicine, chemistry, life sciences and biotechnology areas [1]. Aluminium is an essential metal in organisms present in the world and major response in human life activities and primary key in chemical reactions (enzyme-catalytic reactions and transformations in bio-techniques) [2–4]. Al³⁺ ion exists in different platforms like animals, plants and natural waters. The intake of Al³⁺ in human around ~ 7mg/kg based on the body weight as announced by WHO (World Health Organization) [5,6]. Excessive exposure of aluminium is hazardous to health, which leads to Parkinson's diseases, Alzheimer's diseases, osteomalacia, osteoporosis and breast cancer [7–12]. Due to fragile coordination ability and high hydration ability, the design and development of sensors for Al³⁺ become more challenging and difficult [12–14]. So it is essential to develop a sensor for detection of Al³⁺ in uncomplicated methods with high selectivity. Schiff bases with donor sites such as

nitrogen and oxygen (hard bases) prefers more coordination with hard acid like Al³⁺ [15–22]. Low cost and facile synthesis are advantages of the Schiff bases that enhance an excellent route for the sensing as a fluorescent probes in recent years [23–29].

Coumarin based Schiff bases have excellent role in biological fields [30,31], but past few decades they acted as excellent fluorescent probe for sensing the metal ions. Due to its lower toxicity, easy modification, visible emission wavelength, excellent solubility, high fluorescence quantum yield and good cell permeation [32,33]. Coumarin is the first fluorescent compound that found in humans [29]. The development of excellent fluorescent probes are also based on ICT (intramolecular charge transfer), Excimer mechanism, PET (photoinduced electron transfer), FRET (Fluorescence resonance energy transfer) and C=N isomerization mechanism [34–37]. This made us to focus on coumarin-picolinothiazone Schiff bases, where picolinothiazide acted as a good binder. It has vast application in pharmaceuticals and sensors [38–40]. Isonicotinic acid hydrazide (isoniazid) is an excellent antibiotic mainly for tuberculosis and highly soluble in water. It acts as an effective chemosensors (chromophore) in sensing studies due to magnificent coordination sites (heteroatoms) [41–43]. Kumar et al. [44] synthesized 7-diethylaminoacetyl coumarin isonicotinohydrazone Schiff base

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which acted as sensor for detection of Zn^{2+} ion and Wang et al. [45] designed 3-acetylcoumarinisonicotinohydrazone sensor to detect Al^{3+} ion selectively. Further, Asthana et al. [46] synthesized 1,2-dihydro-7-methoxy-2-oxoquinoline-3-carbaldehydeisonicotinohydrazone also detected the Al^{3+} ion. Herein, we synthesized 7-methoxyacetylcoumarinisonicotinohydrazone probe (**7MIZ**) which selectively senses Al^{3+} ion (fluorescence 'ON'), which has been established by colorimetric titrations and spectral studies.

2. Experimental work

The probe (**7MIZ**) was prepared according to the earlier report [44]. Further, the procedure and instrumentation details were discussed in the supporting information.

3. Results and discussion

7MIZ (Probe)

The preliminary study of the probe (**7MIZ**) was done by the IR spectroscopy. The broad band at 3453cm^{-1} corresponding to $\nu(\text{NH})$ and band at 950cm^{-1} assigned to N-N stretching vibrations [44]. The absorption band at 1700cm^{-1} assigned to C=O group in coumarin ring and the band at 1621cm^{-1} due to $\nu(\text{C}=\text{O})$ group amide [48,49]. A strong absorption band at 1594cm^{-1} due to $\nu(\text{C}=\text{N})$ group [45,47] (Fig. S1). The UV-Vis spectra for the probe showed bands at 227 nm 258 nm and 339 nm assigned to $\pi \rightarrow \pi^*$ transition / $n \rightarrow \pi^*$ transition respectively [50,51]. In proton NMR spectrum, the singlets appeared at δ 2.35 ppm and δ 3.89 ppm corresponding to (N=C- CH_3) proton and methoxy protons respectively [49]. A singlet appeared at δ 11.04 ppm corresponding to (NH-C=O) proton [47]. A sharp singlet at δ 8.23 ppm assigned to C(4) proton and doublets at δ 7.67-7.69 ppm and δ 7.63-7.64 ppm assigned to C(5) and C(6) protons respectively. Singlet at δ 7.80 ppm due to C(8) proton. In pyridine ring, doublets at δ 8.73-8.74 ppm, δ 8.68-8.69 ppm and δ 7.57-7.55 ppm corresponding to C(16), C(17) and C(15) protons respectively and doublet at δ 6.99-7.01 ppm assigned to C(18) proton (Fig. S2). In ^{13}C NMR, singlets appeared at δ 17.05 ppm and δ 56.54 ppm assigned to ($-\text{CH}_3$) carbon atom and methoxy carbon atom respectively. Singlet at δ 163.55 ppm to NH-C=O group and δ 156.02 ppm assigned to (N=HC), δ 100.66 ppm to δ 159.66 ppm corresponding to carbon atoms present in the aromatic regions [44] (Fig. S3). Mass spectrum of (**7MIZ**) were found to be (m/z) 338.30 assigned to $[\text{M}+\text{H}]^+$ (Fig. S4).

4. Single crystal X-ray diffraction study

The single X-ray crystal structure was solved by Olex2 with the olex2.solve structure solution program, using the method of Charge Flipping solution at the temperature of 273 K and refined (olex2.refine) by Gauss-Newton minimization. The suitable crystals mounted on a Bruker APEX-II CCD diffractometer using perfluoroether oil. The structure of needle shaped crystals (**7MIZ**) obtained from methanol/chloroform (1:1v/v) was determined by single crystal X-ray diffraction study. The probe (**7MIZ**) crystallized in triclinic crystal system with the space group P -1. The crystallographic data and ORTEP diagram are given in Table. 1 and Fig. 1>. The hydrogen bonding O(2) N(2) was observed between with the

Table 1
Crystallographic data of Probe (**7MIZ**).

Identification code	Probe (7MIZ)
Empirical formula	$\text{C}_{18}\text{H}_{15}\text{N}_3\text{O}_4$
Formula weight	337.34
Temperature	273 K
Wavelength	0.71073Å
Crystal system	Triclinic
Space group	P -1
Unit cell dimensions	
a	6.7165(2) Å
b	9.5738(3) Å
c	12.6792(5) Å
α	81.9000(10)
β	80.5640(10)
γ	82.5320(10)
Volume	791.47(5) Å ³
Z	2
Density	1.4154Mg/m ³
Absorption coefficient	0.102 mm ⁻¹
F(000)	352.1893
θ range for data collection	2.16 to 27.13°
Limiting indices	-8 ≤ h ≤ 8, -12 ≤ k ≤ 11, -16 ≤ l ≤ 16
Reflections collected	5218
Independent reflections	3484 [R(int) = 0.0269]
Refinement method	Full-matrix least-squares on F ²
Data/restraints/ parameters	2597/228/0
Goodness-of-fit on F ²	1.0618
Final R indices [I > 2σ(I)]	R1 = 0.0515, wR2 = 0.1542
R indices (all data)	R1 = 0.0693, wR2 = 0.1695

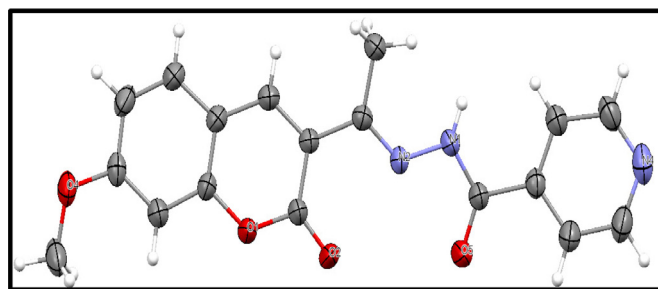


Fig. 1. ORTEP diagram of Probe (**7MIZ**)(thermal ellipsoid at 50 % probability).

bond distance of 2.674 Å. The bond distances of C(6)-N(2), N(1)-N(2), N(1)-C(5) are 1.303(2) Å, 1.3653(17) Å and 1.336(2) Å respectively [41].

5. Colorimetric studies

The colorimetric experiments of the probe (**7MIZ**) was carried out with various metal ions Al^{3+} , Cr^{3+} , Ca^{2+} , Co^{2+} , Cu^{2+} , Fe^{2+} , Mn^{2+} , Ni^{2+} , Hg^{2+} , Zn^{2+} , Na^+ and K^+ at 10 μM concentration in methanol. The solution for the probe and different metal ions (cations) were prepared in methanol (10 μM) separately and further, absorbance and fluorescence (excitation wavelength at 365 nm) studies were carried out for each solutions separately.

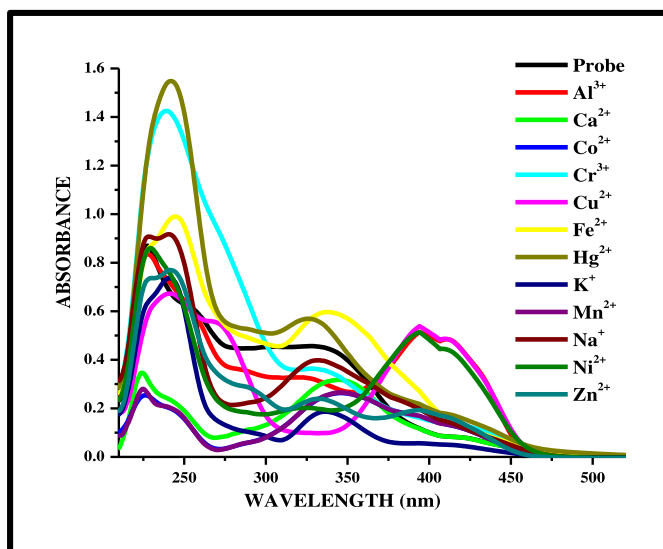


Fig. 2. Absorbance spectra of Probe (7MIZ) in the presences of different Cations in methanol (10 μ M).

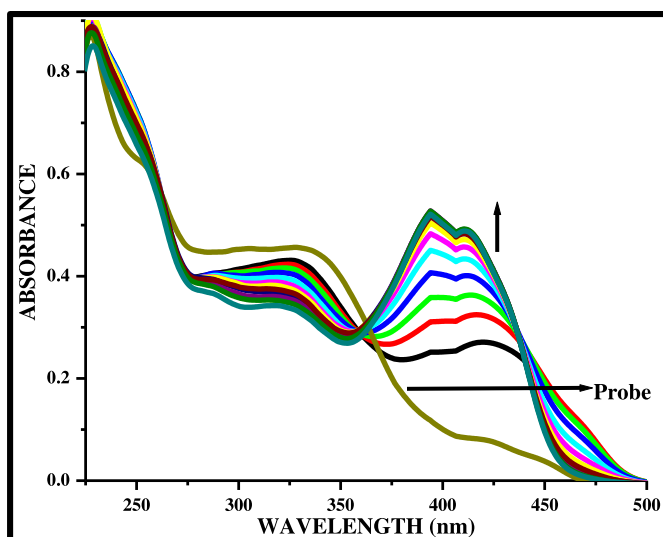


Fig. 3. Absorbance spectra of Probe (7MIZ) upon gradual addition of Al³⁺ ion (0.1 to 1.0 equiv.) in methanol (10 μ M).

5.1. Absorbance study

The UV-Vis spectral analysis was recorded for the probe (7MIZ) and in the presence of various metal ions (10 μ M) in methanol (Fig. 2). In probe (7MIZ), the absorption band at 227 nm assigned to $\pi \rightarrow \pi^*$ transition, the band at 258 nm and 339 nm corresponding to $n \rightarrow \pi^*$ transition. This may be due the presence of pyridine (p-p*) ring in the probe [45]. The titrations were carried out for the probe with Al³⁺ ion was recorded (1 to 10 equivalents) by gradually increasing the concentration of Al³⁺ ion shown in Fig. 3. While increasing the concentration of Al³⁺ ion, the band at 339 nm slightly shifted to 320 nm showed hyperchromism with blue shift and a new absorption band appeared at 393 nm and 411 nm indicated the formation of 7MIZ-Al³⁺ complex, having isosbestic point at 359 nm.

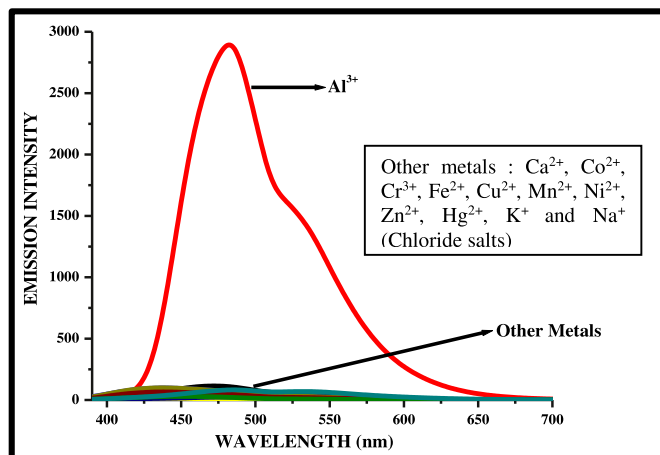


Fig. 4. Fluorescence spectra of Probe (7MIZ) in presences of various cations (chloride salts) in methanol (10 μ M).

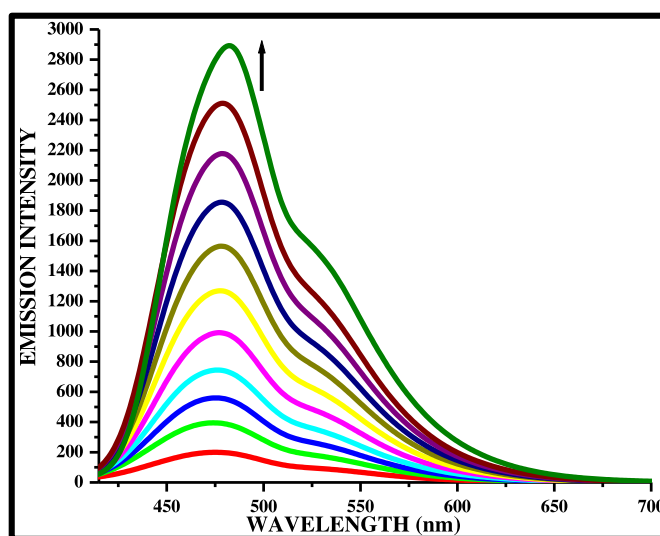


Fig. 5. Fluorescence spectra of Probe (7MIZ) upon gradual addition of Al³⁺ ion (0.1 to 1.0 equiv.) in methanol (10 μ M).

5.2. Fluorescence study

Emission spectra were recorded for the probe (7MIZ) and along with various metal ions to examine the sensing ability of it. Among the various metal ions, the probe selectively senses Al³⁺ ion at emission wavelength of 482 nm and there was no appreciable change in the intensity with other metals (Cr³⁺, Ca²⁺, Co²⁺, Cu²⁺, Fe²⁺, Mn²⁺, Ni²⁺, Hg²⁺, Zn²⁺, Na⁺ and K⁺) (Fig. 4). As the probe added to the Al³⁺ ion, there was a drastic enhancement in the emission intensity showed fluorescence 'ON' behavior of the probe (Fig. 5). Further, the emission intensity get shifted from 474 nm to 482 nm (red shift of 8 nm) which conformed the coordination of Al³⁺ ion to the probe (7MIZ). The change in emission intensity may be clearly explained by PET (photo-induced electron transfer) mechanism. The quenched intensity of the probe was due to the presence of nitrogen atom (lone pair of electrons) leads to PET process. The emission intensity enhanced by addition of Al³⁺ ion to the quenched probe (7MIZ) contributed to CHEF (chelation enhanced fluorescence) effect, which inhibited the PET mechanism. As the probe (7MIZ) was added to Al³⁺ ion (10 μ M concentration) in a vial, the solution turned to be fluorescent, whereas in other metals (Cr³⁺, Ca²⁺, Co²⁺, Cu²⁺, Fe²⁺, Mn²⁺, Ni²⁺, Hg²⁺, Zn²⁺, Na⁺ and K⁺) did not bring any changes under normal visualization

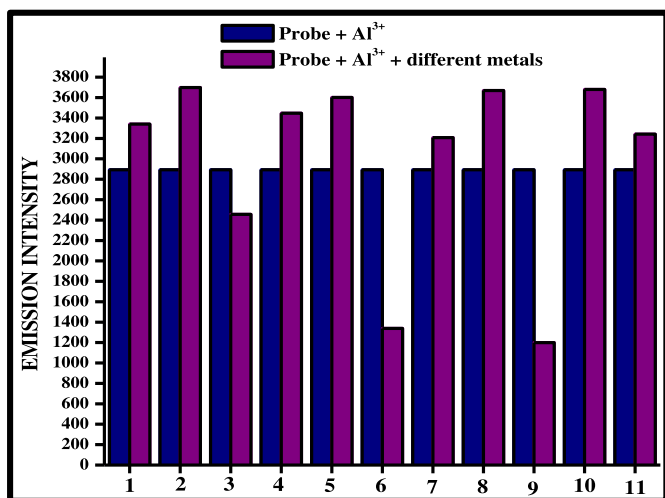


Fig. 6. Fluorescence spectra of 7MIZ- Al^{3+} with various metal ions 1- probe + Al^{3+} + Zn^{2+} ; 2- probe + Al^{3+} + Co^{2+} ; 3- probe + Al^{3+} + Ni^{2+} ; 4- probe + Al^{3+} + Mn^{2+} ; 5- probe + Al^{3+} + Na^+ ; 6- probe + Al^{3+} + Cu^{2+} ; 7- probe + Al^{3+} + Cr^{3+} ; 8- probe + Al^{3+} + Ca^{2+} ; 9- probe + Al^{3+} + Fe^{2+} ; 10- probe + Al^{3+} + Hg^{2+} and 11- probe + Al^{3+} + K^+ .

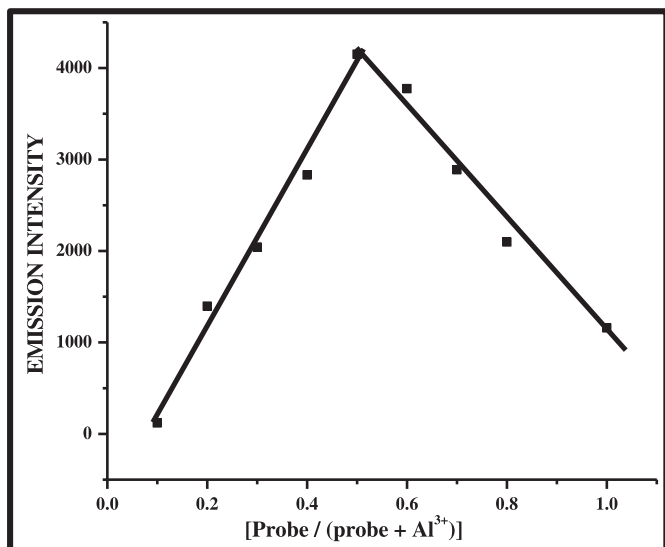


Fig. 7. Job's plot of Probe/[Probe + Al^{3+} ion] in methanol (10 μM).

shown in **Fig. S5**. From the above, it was clearly evident that Al^{3+} ion showed fluorescence 'ON' behavior and further it is confirmed under UV-Vis detection shown in **Fig. S6**.

The competition studies were carried out by using probe (7MIZ)- Al^{3+} with other metal ions such as Cr^{3+} , Ca^{2+} , Co^{2+} , Cu^{2+} , Fe^{2+} , Mn^{2+} , Ni^{2+} , Hg^{2+} , Zn^{2+} , Na^+ and K^+ to examine the interference of them. Cu^{2+} and Fe^{2+} ions showed decrease in the emission intensity by influencing 7MIZ- Al^{3+} and there was no significant interference of other metal ions like Cr^{3+} , Ca^{2+} , Co^{2+} , Mn^{2+} , Ni^{2+} , Hg^{2+} , Zn^{2+} , Na^+ and K^+ when 7MIZ- Al^{3+} added to them (**Fig. 6**) and the emission intensity values are listed in **Table S1**.

6. Job's plot

The stoichiometric binding behavior of the probe (7MIZ) with Al^{3+} ion were investigated by using the job's plot analysis (continuous variation method). It revealed 1:1 stoichiometry between Al^{3+} ion and probe (7MIZ) (**Fig. 7**). It was further confirmed by

Table 2

Comparison of sensing behaviour of reported coumarin based probes with the probe 7MIZ.

Compound	Studies
i) Wang et al. designed a sensor [45] Probe -(3-acetylcoumarinisonicotinohydrazone)	senses Al^{3+} ion selectively. Fluorescence 'ON' LOD value = 0.126 μM Binding constant = $3.11 \times 10^7 \text{ M}^{-1}$
ii) Kumar et al. synthesized a sensor [44] Receptor-(7-diethylamino acetylcoumarin isonicotinohydrazone)	senses Zn^{2+} ion selectively. Fluorescence 'ON' LOD value = $3.26 \times 10^{-9} \text{ M}$ Binding constant = $(1.89 \pm 0.18) \times 10^7 \text{ M}^{-1}$
iii) Kuwar et al. designed a sensor [43] Receptor-(2,4-Dihydroxybenzaldehyde isonicotinohydrazone)	senses Al^{3+} and Cu^{2+} ion selectively. Fluorescence 'ON' LOD value = 1.9 μM Binding constant = $4.8 \times 10^4 \text{ M}^{-1}$
iv) Asthana et al. synthesized a sensor [46] Receptor-(1,2-dihydro-7-methoxy-2-oxoquinolene-3-carbaldehydeisonicotinohydrazide)	senses Al^{3+} ion selectively. Fluorescence 'ON' LOD value = $5.60 \times 10^{-10} \text{ M}$ Binding constant = 695 M^{-2}
This work (7MIZ) V) Probe-(7-methoxy acetylcoumarin isonicotinohydrazone)	senses Al^{3+} ion selectively. Fluorescence 'ON' LOD value = 0.0490 μM Binding constant = $3.6800 \times 10^4 \text{ M}^{-1}$

mass spectroscopy, which showed peak at (m/z) 486.09 assigned to $(7\text{MIZ}-\text{Al}^{3+} + \text{CH}_3\text{OH} + \text{H}_2\text{O})[\text{M}+2\text{H}]^+$ (**Fig. 8**).

7. LOD and binding constant calculation

The Limit of Detection (LOD) was calculated for the probe (7MIZ) and Al^{3+} ion based on the fluorescence titration by using the formula $3\sigma/S$, where 'S' stands for slope between sample concentration versus fluorescence intensity and ' σ ' stands for standard deviation of blank measurements (**Fig. S7**). The LOD was found to be 0.0490 μM . The binding constant value for the probe (7MIZ) - Al^{3+} ion were calculated using the Benesi-Hildebrand equation $[1/(F-F_{\min}) = 1/(K(F_{\max}-F_{\min}))[\text{Al}^{3+}] + 1/(F_{\max}-F_{\min})]$, where F, F_{\min} and F_{\max} are fluorescence intensities of the probe (7MIZ) and in presence of Al^{3+} ion. The association constant K_a constant was found to be $3.6800 \times 10^4 \text{ M}^{-1}$ (**Fig. S8**). Some of the similar reports were compared with our work (**Table 2**).

8. Reversibility and quantum studies of the probe (7MIZ) and probe + Al^{3+} ion

The reversibility of the Probe- Al^{3+} was performed by using EDTA (ethylenediamine tetraacetic acid). To the Probe- Al^{3+} (1 equiv.), EDTA (1 equiv.) was added, the emission intensity enhanced. Again to this solution 2 equiv. of Al^{3+} ion were added, the intensity get increased and to this excess EDTA were added, immediately the intensity get quenched. The reversibility of the probe indicates the selective reponse environmentally and biologically with the Al^{3+} ion sensed metal ion (**Fig. 9**).

The quantum yield (Φ) of the Probe (7MIZ) and Probe with Al^{3+} ion were determined using the equation,

$$\Phi_{\text{sample}} = \left\{ \frac{(\text{OD}_{\text{standard}} \times A_{\text{sample}} \times \eta^2_{\text{sample}})}{(\text{OD}_{\text{sample}} \times A_{\text{standard}} \times \eta^2_{\text{sample}})} \right\} \times \Phi_{\text{standard}}$$

where A is the area (emission spectral curve), OD is the optical density and ' η ' is the refractive index of the solvent. The quantum yield were recorded with the standard quinine sulphate ($\Phi = 0.54$). The quantum yield of the Probe (7MIZ) were found to be $\Phi = 0.0045$ and in the presence of Al^{3+} ion of $\Phi = 0.512$ (increase of 280 folds).

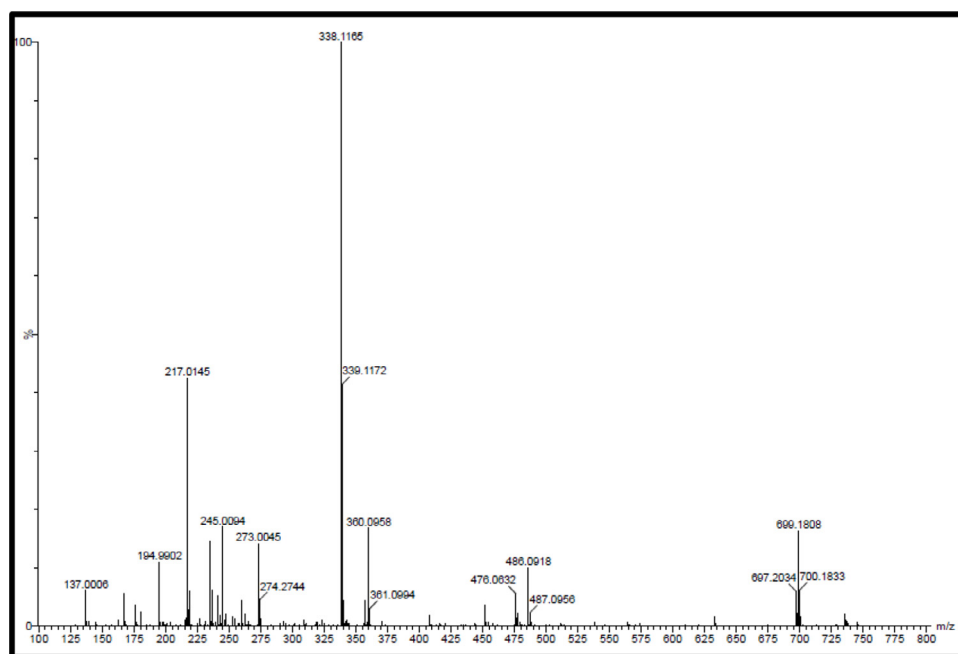


Fig. 8. Mass spectrum of probe- Al^{3+} complex.

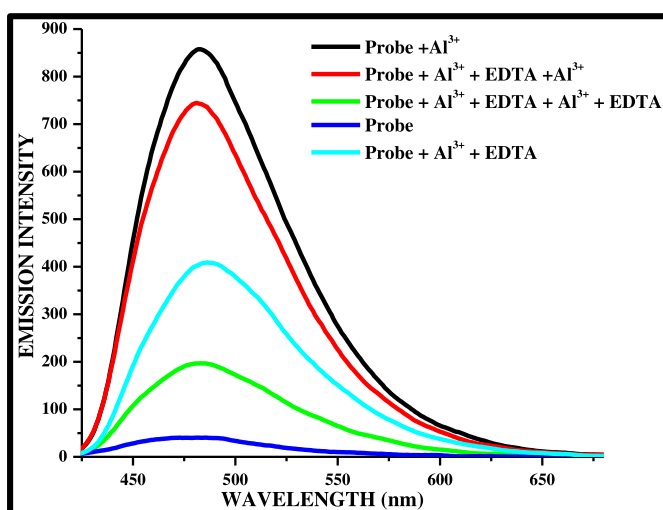


Fig. 9. Reversibility study using probe- Al^{3+} complex with EDTA in Methanol.

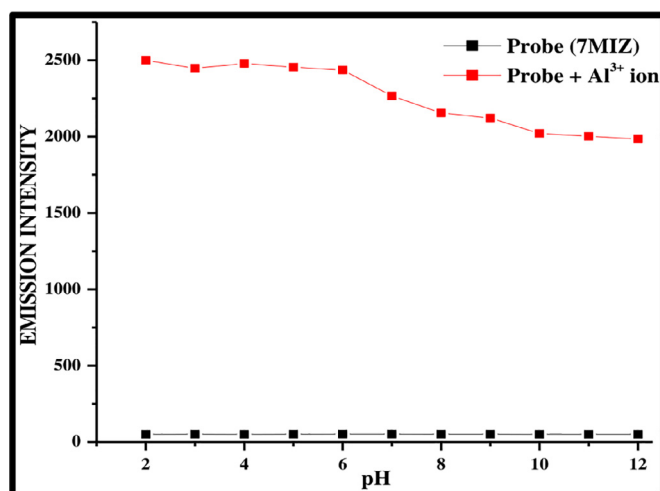


Fig. 10. pH values of Probe (7MIZ) and Probe + Al^{3+} ion.

9. Effect of pH

The effect of pH was studied for the probe and probe + Al^{3+} (from 2 to 12 range) by using sodium hydroxide and hydrochloric acid. There was no significant change in the pH of the probe, the emission intensity remains almost same as the pH were increased. In the presence of Al^{3+} , pH range from 2 to 6 there was no appreciable changes in the intensity under acidic condition. The pH at 7 to 12 the emission intensity decreased slightly may be due to deprotonation that took place during complexation with Al^{3+} ion. Thus from the above result, the probe remains steadily and detect Al^{3+} ion from the pH range 2 to 12 (Fig. 10).

10. Time variation and solvatochromic effect

The effect time variation of Probe in the presence of Al^{3+} ion were carried at the different time intervals (5 min, 10 min, 15 min, 20 min, 25 min, 30 min and 1hr) on the emission spectral studies.

There was no appreciable change in the emission intensity, as the time interval increased (Fig. 11).

The photophysical properties of the probe (7MIZ), the emission spectra were recorded with different solvents with different polarities such as acetone, acetonitrile, methanol, ethanol, chloroform, n-hexane, toluene, DMF and DMSO. Upon excitation at 365 nm, the solvents like acetone, acetonitrile, chloroform, n-hexane, DMF and DMSO, the emission intensity were too weak (lower energy). Unlike, toluene showed three bands with wavelength of 405 nm, 427 nm and 452 nm with lower emission intensity comparability with methanol, showed single emission band with higher wavelength at 482 nm which contributed to ESIPT process due to the intermolecular hydrogen bonding that take place in the molecules (Fig. S9).

11. ^1H NMR Titration

^1H NMR spectra were recorded using DMSO- d_6 at frequency of 400 MHz. Al^{3+} ion was added gradually (0.25 to 1.0 equivalents) to

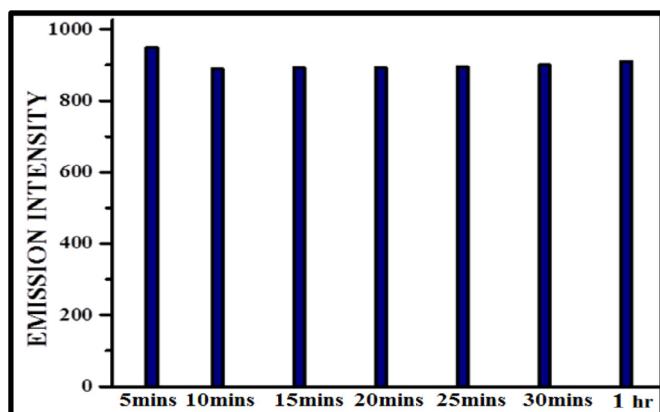


Fig. 11. Time variation of Probe (7MIZ) in the presence of Al^{3+} ion.

the probe (7MIZ) (Fig. 12). The signal at δ 11.04 ppm corresponding to (NH-C=O) proton in the probe, started to disappear while increasing the concentration of Al^{3+} ion which indicated the complexation took place prior to the deprotonation via enolisation. In probe, the singlet appeared at δ 2.35 ppm assigned to (N=C-CH₃) proton underwent an upfield shift while gradually increasing the concentration Al^{3+} ion which indicated the coordination of azomethine nitrogen atom. Hence, the coordination of probe with Al^{3+} ion took place via oxygen atom (C=O) in coumarin ring, azomethine nitrogen atom (N=C-CH₃) and oxygenation (NH-C=O) of amide revealed five coordination of 7MIZ- Al^{3+} complex.

12. IR spectrum of 7MIZ- Al^{3+} complex

In IR spectrum, the band at 1700 cm^{-1} due to C=O group in coumarin ring was shifted to 1653 cm^{-1} indicating the coordination of C=O group in complexation [47]. The strong band at 1594 cm^{-1} due to $\nu(\text{C}=\text{N})$ group was shifted to 1552 cm^{-1} showing the bonding of azomethine nitrogen in 7MIZ- Al^{3+} complex and band at 1621 cm^{-1} due to amide $\nu(\text{C}=\text{O})$ group got disappeared and new band appeared at 1394 cm^{-1} corresponds to C-O indicated the co-

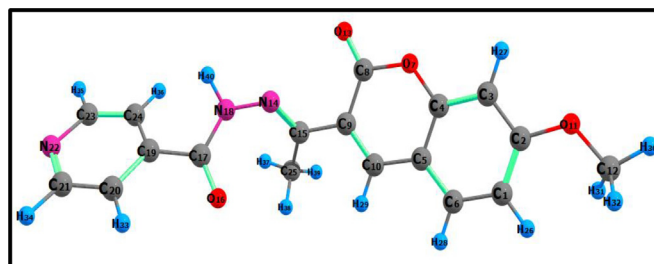


Fig. 13. Optimized structure of the Probe (7MIZ).

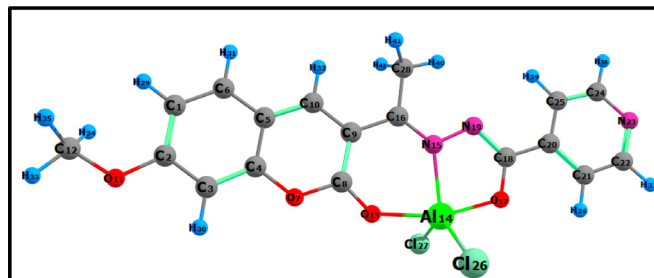


Fig. 14. Optimized structure of the 7MIZ- Al^{3+} complex.

ordination of oxygenation after enolisation [44] (Fig. S10). From the spectroscopic analysis, it has been found that the probe (7MIZ) coordinated to Al^{3+} ion in monobasic tridentate manner.

13. Proposed mechanism

Based on the spectral and theoretical data (IR, UV-Vis, $^1\text{H-NMR}$ and Mass) and Job's plot (1:1 stoichiometry) the following structure of 7MIZ- Al^{3+} complex has been proposed.

14. Theoretical calculations

In order to confirm the formation of Probe (7MIZ) and (7MIZ)- Al^{3+} complex, theoretical calculations were done by B3LYP and

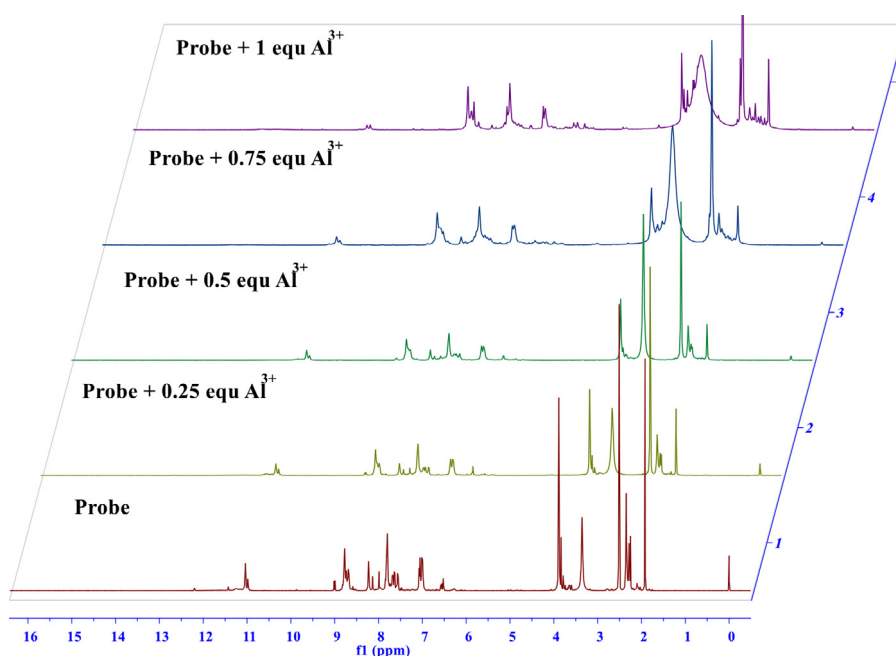


Fig. 12. $^1\text{H-NMR}$ titration spectra of Probe with different equivalents of Al^{3+} ion.

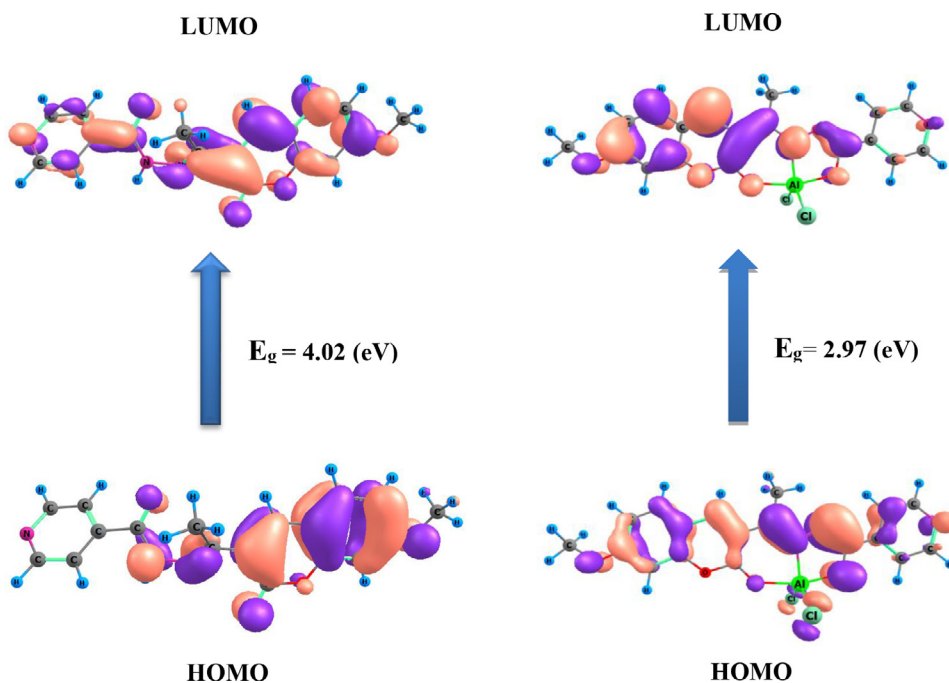


Fig. 15. HOMO-LUMO energy levels of Probe (7MIZ) and 7MIZ-Al³⁺ complex were calculated from B3LYP level of theory.

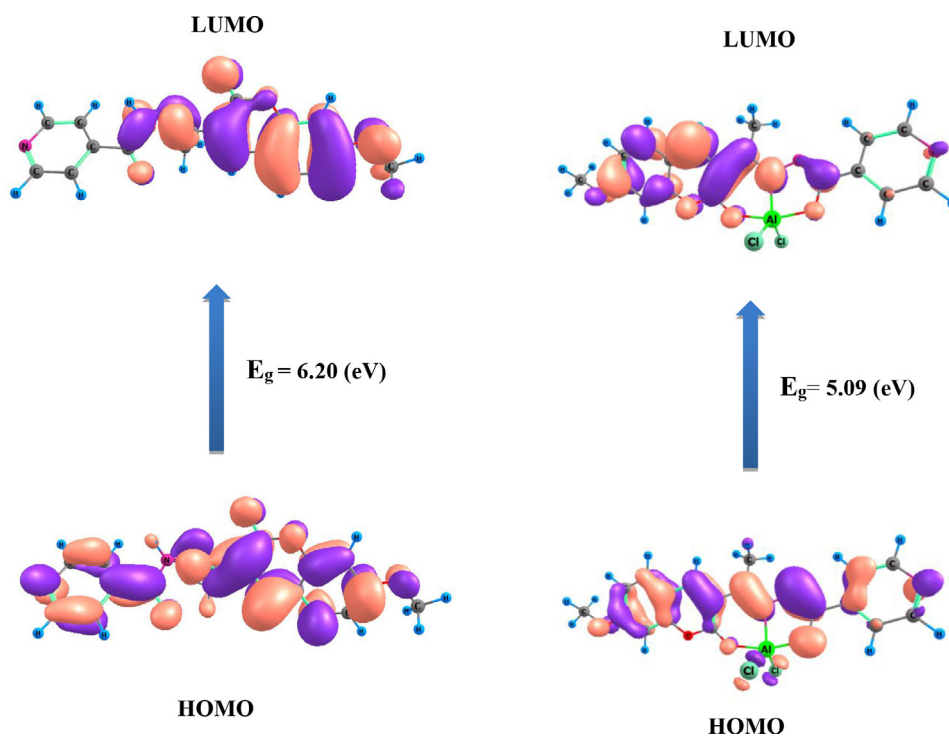


Fig. 16. HOMO-LUMO energy levels of Probe (7MIZ) and 7MIZ-Al³⁺ complex were calculated from M06-2X level of theory.

M06-2X level of theories. The spectroscopic studies (IR and UV) obtained for the probe and probe with Al³⁺ ion through theoretical calculations were similar to the experimental values. The detailed description of the energy of transition, wavelength and orbitals involved in the Probe (7MIZ) were represented in Table S2. In experimental, IR spectral frequencies for C=O, C=N and C-O were found as 1653 cm⁻¹, 1552 cm⁻¹ and 1394 cm⁻¹ respectively whereas in theoretical studies the stretching frequency for C=O, C=N and C-O were found as 1655 cm⁻¹, 1536 cm⁻¹ and 1320 cm⁻¹ in B3LYP and in M06-2X, the stretching vibrations were found at 1699 cm⁻¹,

1588cm⁻¹ and 1350 cm⁻¹ indicates the formation of 7MIZ-Al³⁺ complex (Fig. S11). In UV-Vis spectrum, the bands at 227 nm ($\pi \rightarrow \pi^*$ transition), 258 nm and 320 nm ($n \rightarrow \pi^*$ transition), 393 nm and 411 nm confirmed the formation of 7MIZ-Al³⁺ complex. This is in good agreement with the calculated values through B3LYP and M06-2X methods. In B3LYP, the bands at 254 nm and 421 nm were observed and the corresponding orbital transitions from H⁻⁹-LUMO (39%), H⁻⁴-L+1 (20%), HOMO-L+3 (34%) and HOMO-LUMO (99%) respectively. However, in M06-2X method, the bands at 205 nm (orbital transitions from H⁻⁹-LUMO (12%), H⁻⁷-LUMO (34%),

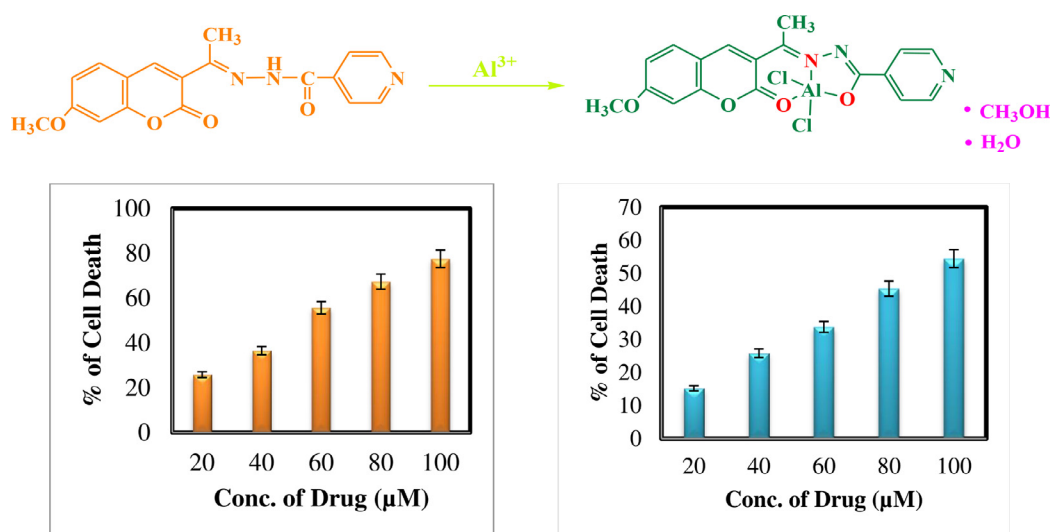


Fig. 17. MTT assay using (MDA-MB-231) cell line. A plot of cell death vs concentration A. Probe (7MIZ) and B. 7MIZ-Al³⁺ complex.

H⁻⁸-LUMO (9%), 262 nm((H⁻¹-LUMO (43%), HOMO-L+1(39%) and 358 nm (HOMO-LUMO (95%) were observed (Fig. S12 and Table S3).

The optimized structure of the Probe (7MIZ) and 7MIZ+Al³⁺ complex has been given in (Figs. 13 and 14). The coordination took place through i) coumarin oxygen atom (O13) with bond distance of 1.964 Å ii) azomethine nitrogen atom (N=C-CH₃) (N15) with bond distance of 2.085 Å and iii) (C-O) in amide group (O17) with bond distance of 1.871 Å which are observed in B3LYP. However in M06-2X, the bond distances for O(13), N(15) and O(17) were found to be 1.961 Å, 2.056 Å and 1.859 Å respectively. In both cases M06-2X and B3LYP, LUMO was delocalized on the coumarin ring through carbon, oxygen, nitrogen atoms of the probe (7MIZ) and on other hand, HOMO was localized on the Al³⁺ coordinated with chloride atom and pyridine ring of carbon and oxygen atom of amide (C-O) group. Wherein coordination takes place in monobasic tridentate manner and the influence of Al³⁺ ion to the probe (7MIZ) leads to chelation enhanced fluorescence effect, inhibiting the PET mechanism. The obtained bond angles and bond distances were given in (Table S4 and S5). The E_g (band gap energy) value were calculated from HOMO and LUMO energy levels (ie., E_g = E_{LUMO} - E_{HOMO}). The band gap energy (E_g) in B3LYP was found as 4.02 eV for probe and 2.97 eV in the presence of Al³⁺ ion and in M06-2X method E_g value found as 6.20 eV for probe and 5.09 eV for the complex (Fig. 15) 7MIZ+Al³⁺ shown in Fig. 16 and Table S6. From the above results, the complex 7MIZ+Al³⁺ showed lower frontier orbital gap ie., more polarizable and reactive complex, than the Probe (7MIZ), indicating the bathochromic shift with maximum absorption of probe binding with Al³⁺ metal ion. The band gap energy for complex (7MIZ-Al³⁺) in M06-2X is comparably higher than in B3LYP. [2,52,53]

15. MTT Assay

The cytotoxic effects of the Probe (7MIZ) and 7MIZ-Al³⁺ complex were determined by Breast cancer cell line (MDA-MB-231). The cells were cultured (1 × 10⁴ cells/well) with or without the drug (20 μM, 40 μM, 60 μM, 80 μM and 100 μM) for 24 h. The plated cells were incubated with 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (0.5 mg/ml) for 4 hrs at 37°C. After incubation, the plates were at room temperature placed for 20 min with constant shaking to get complete dissolution of formazon and the absorbance was recorded at 570 nm in UV spectrophoto-

metric plate reader. IC₅₀ value were calculated for the Probe (7MIZ) and 7MIZ-Al³⁺ complex using % inhibition = [mean OD of untreated cells (control)/mean OD of treated cells (control)] × 100 and the graph was plotted against cell death versus concentration of the drug. IC₅₀ value for the Probe (7MIZ) and 7MIZ-Al³⁺ complex were found to be 90.78 μM and 56.19 μM respectively. From the above result, the complex 7MIZ-Al³⁺ showed better cytotoxicity than the Probe (7MIZ) (Fig. 17).

16. Conclusion

Coumarin based Schiff base (7-methoxy acetyl coumarin isonitotinohydrazone (7MIZ)) probe was designed and characterized by various spectral studies and X-ray crystallographic investigation confirmed its structure. The probe selectively senses Al³⁺ ion among the various other metal ions. Evidently, mass spectral data and Job's plot showed 1:1 stoichiometry of 7MIZ-Al³⁺ complex and coordination takes place in monobasic tridentate (O,N,O) type. The association constant value (3.6800 × 10⁴ M⁻¹) and detection value (0.0490 μM) were calculated. The DFT studies were carried out by B3LYP and M06-2X level of theory for the Probe (7MIZ) and 7MIZ-Al³⁺ complex to confirm its molecular structure in which complex showed more reactive than Probe in both the cases. 7MIZ-Al³⁺ complex showed high cytotoxic effect than the Probe (7MIZ) against MDA-MB-231 cell line.

Supporting information

Crystallographic data for the probe 7MIZ (CCDC No. 2184380) was deposited at the Cambridge Crystallographic centre as supplementary publication. The data can be obtained free of charge at W. W. W.ccdc.cam.ac.uk/conts/retrieving.html/

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

D. Ravichandran: Conceptualization, Methodology, Software, Validation, Data curation, Writing – original draft, Visualization,

Writing – review & editing. **M. Ranjani**: Methodology, Software, Writing – original draft, Writing – review & editing. **G. Prabu Sankar**: Methodology, Software, Data curation. **R. Shankar**: Methodology, Software, Validation, Data curation. **M. Karthi**: Software, Validation, Data curation. **S. Selvakumar**: Software, Validation, Data curation. **R. Prabhakaran**: Conceptualization, Methodology, Supervision, Investigation, Validation, Project administration.

Data Availability

Data will be made available on request.

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Supplementary materials

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Reference

- [1] Y.J. Tong, L.D. Yu, L.L. Wu, S.P. Cao, Y.L. Guo, R.P. Liang, J.D. Qiu, Ratiometric detection of Cu^{2+} using luminol-Tb-GMP nanoprobe with high sensitivity and selectivity, *ACS Sustain. Chem. Eng.* 6 (2018) 9333–9341.
- [2] G. Kalaiarasi, M. Ranjani, R. Prabhakaran, P.R. Athira, A. Kosika, A novel coumarin based probe for Al(III): synthesis, spectral characterization, photophysical properties, DFT calculations and fluorescence cellular bio-imaging, *Inorg. Chim. Acta* 535 (2022) 120–846.
- [3] S. Dey, R. Purkait, K. Pal, K. Jana, C. Sinha, Aggregation-induced emission-active hydrazide-based probe: selective sensing of Al^{3+} , HF^{2-} and nitro explosives, *ACS Omega* 4 (2019) 8451–8464.
- [4] L.M. Liu, Z.Yin Yang, A new off-on fluorescent sensor for the detection of Al(III) based on a chromone-derived Schiff-base, *Inorg. Chim. Acta* 469 (2018) 588–592.
- [5] C.I. David, N. Bhuvanesh, H. Jayaraj, A. Thamilselvan, D. Parimala devi, A. Abiram, J. Prabhu, R. Nandhakumar, Experimental and theoretical studies on a simple S–S-bridged dimeric Schiff base: selective chromo-fluorogenic chemosensor for nanomolar detection of Fe^{2+} & Al^{3+} ions and its varied applications, *ACS Omega* 5 (2020) 3055–3072.
- [6] D. Aydin, S. Dinckan, S. Nihan K. Elmas, T. Savran, F.N. Arslan, I. Yilmaz, A novel phenolphthalein-based fluorescent sensor for Al^{3+} sensing in drinking water and herbal tea samples, *Food Chem* 337 (2021) 127659.
- [7] I.Ho Song, P. Torawane, J.S. Lee, S.D. Warkad, A. Borase, S.K. Sahoo, S.B. Nimse, A. Kuwar, *Mater. Adv.* 2 (2021) 6306–6314.
- [8] S.C. Bondy, Low levels of aluminum can lead to behavioral and morphological changes associated with Alzheimer's disease and age-related neuro degeneration, *Neurotoxicology* 52 (2016) 222–229.
- [9] C. Rui Li, S. Liang Li, Z. Yin Yang, A chromone-derived Schiff-base as Al^{3+} “turn-on” fluorescent probe based on photoinduced electron-transfer (PET) and C=N isomerization, *Tetrahedron Lett* 57 (2016) 4898–4904.
- [10] C. Kim, H.J. Jang, J.H. Kang, D. Yun, A multifunctional selective “turn-on” fluorescent chemosensor for detection of Group IIIA ions Al^{3+} , Ga^{3+} and In^{3+} , *Photochem. Photobiol. Sci.* 17 (2018) 1247–1255.
- [11] B.J. Pang, C. Rui Li, Z.Y. Yang, A novel chromone and rhodamine derivative as fluorescent probe for the detection of Zn(II) and Al(III) based on two different mechanisms, *Spectrochim. Acta A* 204 (2018) 641–647.
- [12] P. Ghorai, K. Pal, P. Karmakar, A. Saha, Development of two fluorescent chemosensors for selective detection of Zn^{2+} and Al^{3+} ions in quinoline platform by tuning of substituent in the receptor part: Elucidation of structures of metal bound chemosensors and biological studies, *Dalton Trans.* 49 (2020) 4758–4773.
- [13] L. Fan, T. Rong Li, B. Dui Wang, Z. Yin Yang, C. Jiao Liu, A colorimetric and turn-on fluorescent chemosensor for Al(III) based on a chromone Schiff-base, *Spectrochim. Acta A* 118 (2014) 760–764.
- [14] C.J. Liu, Z.Y. Yang, L. Fan, X. Long Jin, J. Mei An, X. Ying Cheng, B. Dui Wang, Novel optical selective chromone Schiff base chemosensor for Al^{3+} ion, *J. Lumin* 158 (2015) 172–175.
- [15] L. Yan, Y. Ma, M. Cui, Z. Qi, A novel coumarin-based fluorescence chemosensor containing L-histidine for aluminium(III) ions in aqueous solution, *Anal. Methods* 7 (2015) 6133–6138.
- [16] T.J. Jia, W. Cao, X.J. Zheng, L.P. Jin, A turn-on chemosensor based on naphthol-triazole for Al(III) and its application in bioimaging, *Tetrahedron Lett* 54 (2013) 3471–3474.
- [17] B.J. Pang, C.R. Li, Z. Yin Yang, Design of a colorimetric and turn-on fluorescent probe for the detection of Al(III), *J. Photochem. Photobiol. A* 356 (2018) 159–165.
- [18] C. Liu, L.M. Liu, T.R. Li, K. Liu, Z.Y. Yang, A simple fluorescent-colorimetric probe for selective switch-on detection of Al^{3+} in ethanol, *Inorg. Chim. Acta* 502 (2020) 119327.
- [19] L. Fan, J.C. Qin, C.R. Li, Z.Y. Yang, A Schiff-base receptor based chromone derivative: highly selective fluorescent and colorimetric probe for Al(III), *Spectrochim. Acta A* 218 (2019) 342–347.
- [20] L. Tian, J. Xue, S.L. Li, Z.Y. Yang, A novel chromone derivative as dual probe for selective sensing of Al(III) byfluorescent and Cu(II) by colorimetric methods in aqueous solution, *J. Photochem. Photobiol. A* 382 (2019) 111955.
- [21] Z. Kejik, R. Kaplánek, M. Havlík, T. Bříza, D. Vavřínová, B. Dolenský, P. Martásek, V. Král, Aluminium(III) sensing by pyridoxal hydrazine utilizing the chelation enhanced fluorescence effect, *J. Lumin* 180 (2016) 269–277.
- [22] R. Purkait, C. Patra, A.D. Mahapatra, D. Chattopadhyay, C. Sinha, A visible light excitable chromone appended hydrazide chemosensor for sequential sensing of Al^{3+} and F^{-} in aqueous medium and in Vero cells, *Sens. Actuators B* 257 (2018) 545–552.
- [23] R. Das, Bej S. H. Hirani, P. Banerjee, Trace-level humidity sensing from commercial organic solvents and food products by an AIE/ESIPT-triggered piezochromic luminogen and ppb-level “OFF–ON–OFF” Sensing of Cu^{2+} : a combined experimental and theoretical outcome, *ACS Omega* 6 (2021) 14104–14121.
- [24] M. Shellaiah, Y.T. Chen, N. Thirumalaivasan, B. Aazaad, K. Awasthi, K.W. Sun, S.Pao Wu, M.C. Lin, N. Ohta, Pyrene-based AIEE active nanoprobe for Zn^{2+} and tyrosine detection demonstrated by DFT, bioimaging, and organic thin-film transistor, *ACS Appl. Mater. Interfaces* 13 (2021) 28610–28626.
- [25] Y. Wang, X. Hao, L. Liang, L. Gao, X. Ren, Y. Wu, Hongchi Zhao, A coumarin-containing Schiff base fluorescent probe with AIE effect for the copper(II) ion, *RSC Adv* 10 (2020) 6109–6113.
- [26] J. Fu, B. Li, H. Mei, Y. Chang, K. Xu, Fluorescent schiff base probes for sequential detection of Al^{3+} and F^{-} and cell imaging applications, *Spectrochim. Acta A* 227 (2020) 117678.
- [27] T. Hu, L. Wang, J. Li, Y. Zhao, J. Cheng, W. Li, Z. Chang, C. Sun, *Inorg. Chim. Acta* 524 (2021) 120421.
- [28] L. Wang, Y. Zhao, J. Li, C. Sun, W. Li, Z. Chang, D. Qi, Two Schiff-base fluorescent-colorimetric probes based on naphthaldehyde and aminobenzoic acid for selective detection of Al^{3+} , Fe^{3+} and Cu^{2+} ions, *J. Mol. Struct.* 1255 (2022) 132431.
- [29] P. Zhang, X. Xub, Y.F. Cuib, X.H. Weia, S.J. memga, Y.X. Sun, A highly sensitive and selective bisalamo-coumarin-based fluorescent chemical sensor for $\text{Cr}^{3+}/\text{Al}^{3+}$ recognition and continuous recognition S^{2-} , *J. Photochem. Photobiol. A* 408 (2021) 113066.
- [30] G. Kalaiarasi, S.R.J. Rajkumar, S. Dharani, F.R. Fronczek, M.S.A. Muthukumar Nadarb, R. Prabhakaran, Cyclometallated ruthenium(II) complexes with 3-acetyl-2[H]-chromene-2-one derived CNS chelating ligand systems: synthesis, X-ray characterization and biological evaluation, *New J. Chem.* 42 (2018) 336–354.
- [31] M. Li, X. Kong, B. Dong, N. Zhang, W. Song, Y. Lu, W. Lin, A novel two-photon fluorescent probe for detecting FA based on a coumarin derivative and its applications in living cells, zebrafish and tissues, *New J. Chem.* 43 (2019) 11844–11850.
- [32] Y.X. Song, Z. Chen, H.Q. Li, Advances in coumarin-derived fluorescent chemosensors for metal ions, *Curr. Org. Chem.* 16 (2012) 2690–2707.
- [33] L. Wang, Y.F. Li, G.P. Li, Z.K. Xie, B.X. Ye, Electrochemical characters of hycromone at the graphene modified electrode and its analytical application, *Anal. Methods* 7 (2015) 3000–3005.
- [34] S. Erdemir, O. Kocyigit, S. Karakurt, A new perylene bisimide-armed calix[4]-aza-crown as “turn on” fluorescent sensor for Hg^{2+} ion and its application to living cells, *Sens. Actuators B* 220 (2015) 381–388.
- [35] Y. Zhou, K.H. Chu, H.F. Zhen, Y. Fang, C. Yao, Visualizing Hg^{2+} ions in living cells using a FRET-based fluorescent sensor, *Spectrochim. Acta A* 106 (2013) 197–202.
- [36] N.A.S. Pungut, H.M. Saad, K.S. Sim, K.W. Tan, A turn on fluorescent sensor for detecting Al^{3+} and colorimetric detection for Cu^{2+} : Synthesis, cytotoxicity and on-site assay kit, *J. Photochem. Photobiol. A* 414 (2021) 113290.
- [37] P. Saluja, H. Sharma, N. Kaur, N. Singh, D.O. Jang, Benzimidazole-based imine-linked chemosensor: chromogenic sensor for Mg^{2+} and fluorescent sensor for Cr^{3+} , *Tetrahedron* 68 (2013) 2289–2293.
- [38] Z.D. Liu, H.J. Xu, S.S. Chen, L.Q. Sheng, H. Zhang, F.Y. Hao, P.F. Su, W.L. Wang, Solvent-dependent “turn-on” fluorescence chemosensor for Mg^{2+} based on combination of C=N isomerization and inhibition of ESIPT mechanisms, *Spectrochim. Acta A* 149 (2015) 83–89.
- [39] X.Y. Zhang, Y.S. Yang, W. Wang, Q.C. Jiao, H.L. Zhu, Fluorescent sensors for the detection of hydrazine in environmental and biological systems: Recent advances and future prospects, *Coord. Chem. Rev.* 417 (2020) 213367.
- [40] M.A. Haque, R.G. Chaudhary, L.J. Paliwal, Synthesis, structural, morphological, and thermal decomposition kinetics of Iron (II) coordination polymer of sebacyl bis (isonicotinoylhydrazone), *Inorg. Chim. Acta* 462 (2017) 298–307.
- [41] P. Sakhivel, K. Sekar, S. Singaravelu, G. Sivaraman, Rhodamine-isonicotinic hydrazide analogue: a selective fluorescent chemosensor for the nanomolar detection of picric acid in aqueous media, *Chem. Select* 4 (2019) 3817–3822.
- [42] T. Sharif, A. Niaz, M. Najeeb, M.I. Zaman, M. Ihsan, Sirajuddin, Isonicotinic acid hydrazide-based silver nanoparticles as simple colorimetric sensor for the detection of Cr^{3+} , *Sens. Actuators B* 216 (2015) 402–408.
- [43] A. Kuwar, I. Song, P.D. Torawane, J. Lee, S. Warkad, A.U. Borse, S.K. Sahoo, S.B. Nimse, Detection of Al^{3+} and Cu^{2+} ions by isonicotinohydrazide based

- chemosensors and its application to live cell imaging, *Mater. Adv.* 19 (2021) 1–20.
- [44] V. Kumar, A. Kumar, U. Diwan, K.K. Upadhyay, A Zn²⁺-responsive highly sensitive fluorescent probe and 1D coordination polymer based on a coumarin platform, *Dalton Trans* 42 (2013) 13078.
- [45] W. Wang, L. Jin, Y. Kuang, Z. Yuan, Q. Wang, Isonicotinoylhydrazide modified 3-acetylcoumarin scaffold as an efficient chemical reversible sensor to detect Al³⁺ selectively and its application in live cells imaging, *Synth. Commun.* 49 (2017) 2501–2511.
- [46] S.K. Asthana, A. Kumar, Shweta Neeraj, S.K. Hira, P.P. Manna, K.K. Upadhyay, Brightening quinolineimines by Al³⁺ and subsequent quenching by PPI/PA in aqueous medium: synthesis, crystal structures, binding behavior, theoretical and cell imaging studies, *Inorg. Chem.* 56 (2017) 3315–3323.
- [47] R.S. Hunoor, B.R. Patil, D.S. Badiger, R.S. Vadavi, K.B. Gudasi, V.M. Chandrashekar, I.S. Muchchandi, Spectroscopic, magnetic and thermal studies of Co(II), Ni(II), Cu(II) and Zn(II) complexes of 3-acetylcoumarin-isonicotinoylhydrazide and their antimicrobial and anti-tubercular activity evaluation, *Spectrochim. Acta A* 77 (2010) 838–844.
- [48] K Siddappa, K.A. Ganure, Synthesis, Characterization Biological Activities of Some Transition metal complexes with Coumarin Schiff base, *Int. j. Ethics Eng. Manag. Educ.* 1 (2014) 180–186.
- [49] G. Kalaiarasi, S.R.J. Rajkumar, G. Aswini, S. Dharani, F.R. Fronczek, R. Prabhakaran, 3-Acetyl-8-methoxy-2[H]-chromen-2-one derived Schiff bases as potent antiproliferative agents: Insight into the influence of 4(N)-substituents on the in vitro biological activity, *Spectrochim. Acta A* 200 (2018) 246–262.
- [50] G. Kalaiarasi, S.R.J. Rajkumar, S. Dharani, F.R. Fronczek, R. Prabhakaran, Biological evaluation of new organoruthenium(II) metallates containing 3-acetyl-8-methoxy-2H-chromen-2-one appended CNS donor Schiff bases, *J. Organomet. Chem.* 866 (2018) 223–242.
- [51] G. Kalaiarasi, C. Umadevi, A. Shanmugapriya, P. Kalaivani, F. Dallemer, R. Prabhakaran, DNA(CT), protein(BSA) binding studies, anti-oxidant and cytotoxicity studies of new binuclear Ni(II) complexes containing 4(N)-substituted thiosemicarbazones, *Inorg. Chim. Acta* 453 (2016) 547–558.
- [52] X.F. Bao, Q.S. Cao, Y.Z. Xu, Y.X. Gao, Y. Xu, X.M. Nie, B.J. Zhou, T. Pang, J. Zhu, Synthesis and evaluation of a new Rhodamine B and Di(2-picoly)amine conjugate as a highly sensitive and selective chemosensor for Al³⁺ and its application in living-cell imaging *Bioorg. Med. Chem.* 23 (2015) 694–702.
- [53] E. Kavitha, D. Ramarajan, A. Rakic, D. Dimic, S. Sudha, P.N. Nirmala, Structural, spectroscopic, quantum chemical, and molecular docking investigation of (E)-N'-(2,5-dimethoxybenzylidene)picolinohydrazide, *J. Mol. Struct.* 1253 (2022) 132259.