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A highly selective and sensitive turn-on probe for aluminum(III) based on quinoline schiff's base and its cell imaging

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Abstract

A reversible schiff's base fluorescence probe for Al^{3+}, (3,5-dichloro-2-hydroxybenzylidene) quinoline-2-carbohydrazide (**QC**), based on quinoline derivative has been designed, synthesized and evaluated. The **QC** exhibited a high sensitivity and selectivity toward Al^{3+} in EtOH-H_2O (v/v=1:9, pH=6) by forming a 1:1 complex with Al^{3+} and the detection limit of **QC** for Al^{3+} was as low as 0.012 μM. Furthermore, these results displayed that the binding of **QC**-Al^{3+} was broken by F^-, so this system could be used to monitor F^- in the future. The enhancement fluorescence of the **QC** could be attributed to the inhibition of PET and ESIPT and the emergency of CHEF process induced by Al^{3+}. More importantly, **QC** was not only successfully used for the determination of trace Al^{3+} in the tap water and the human blood serum, but was valid for fluorescence imaging of Al^{3+} in the Hela cells.

Keywords：fluorescence probe，aluminum ions，schiff's base，cell imaging

1. Introduction

There are huge metal elements contained in earth and aluminum is the most affluent one. Aluminum compounds play a significant role in daily life[1], industry[2]

and agriculture[3]. Excessive Al^{3+} ions are not only harmful to growing plants[4], but may give rise to a lot of illnesses, for example, Parkinson's disease[5], Alzheimer's disease[6] and osteoporosis[7]. On the other hand, after absorption, aluminum would accumulate in the body[8]. In this way, although trace amounts of aluminum ions exist in the drinking water, low-dose chronic exposure to the ions may cause damage. So, the detection of Al^{3+} has become research focus recently [9-11]. Among various methods, the fluorescent probes has attracted more significant interests[8-10, 12, 13] , due to its several outstanding advantages of simplicity, rapidity, high sensitivity and selectivity[14, 15]. But, it is more difficult to recognize Al^{3+} than other metal ions by fluorescence method because of its poor coordination ability and spectroscopic characteristics[16]. Generally, Al^{3+} ions, as a hard acid, tend to coordinate with ligands with hard-base donor sites. Moreover, the Schiff's base with rich nitrogen-oxygen coordination can offer a hard-base environment, which will provide enough binding sites and improve the identification of probe for hard-acid metal [17]. Recently, a lot of Schiff's base compounds have been reported as a probe for the detection of aluminum ion by fluorescence [13, 18-23]. The majority of the reported Al^{3+} probes, however, have disadvantages including only application in water sample[24] or cell imaging [8, 19] and/or existing interference from other metal ions (such as, Fe^{3+}, Ni^{2+}, Cu^{2+})[19, 20] and/or the higher rate of organic solvent in the detection system[13, 21-23] and/or higher detection limit[13, 19]. Along those lines, those probes were restricted application of water samples and biological systems.

Meanwhile, a fluorescence probe based on two or more mechanisms may be more valuable because it can provide multiple signals and improve selectivity and sensitivity[25-27]. But most of the recent years reported probes for Al^{3+} are established on single signal mechanism[16, 28-30], which is intramolecular charge transfer (ICT)[30], photo induced electron transfer (PET)[28] and excited-state intramolecular proton transfer (ESIPT)[29]. For now, the development of the fluorescence probe for Al^{3+} in water solution and cell with high selectivity and sensitivity remains a difficult challenge. Obviously, Schiff's base ligands with a

proton acceptor (–C=O, –N=) and a proton donor (–OH, –NH–) group can produce the ESIPT process[31]. In the meantime, lone pair electrons from the nitrogen atom (–C=N) of Schiff's base ligands can induce PET process[32]. In addition, fluorescence probe with Schiff's base chelated metal ions would exhibit a chelation-enhanced fluorescence (CHEF) process[33]. And the quinoline is usually used as a plotform to construct probe for metal ion. Modifying the quinoline could easily give the probe with the group of –OH, –NH–,–C=O, –N=, –C=N[34], which could not only satisfy a prerequisite for the design of a probe based on more mechanisms but also improve the water solubility of fluorescent probe.

Keeping these in mind, a novel schiff's base fluorescence probe (3,5-dichloro-2-hydroxybenzyli-dene) quinoline-2-carbohydrazide(**QC)** has been designed for Al^{3+}. The fluorescent probe **QC** showed a high selective toward Al^{3+}. Furthermore, the binding of **QC**-Al^{3+} could be reversed by F^-. More importantly, these results revealed that the probe **QC** was used to detect Al^{3+} in human blood serum and image Al^{3+} in HeLa cells.

2. Experimental

2.1 Equipment and material

The spectra of UV-Vis and fluorescence were gained through a Hitachi U-3900 (Japan) and a Hitachi F-7000(Japan), respectively, with a 1cm length and 4mL quart optical cell. ^{1}H NMR was taken on a Bruker 400MH_Z in $CDCl_3$ or DMSO-d_6 with TMS as the internal standard (Switzerland). The spectra of mass were recorded on Thermo Fisher scientific LTQ FT Ultra mass spectrometer (America). The melting point was determined on X-4 microscope melting point (China). The analyses of elementary were realized by a Vario EL Ⅲelementary analysis instrument (Germany). The pH was obtained on a Model pHs-3C meter (China). The imaging of HeLa cells was gained on a Nikon ECLIPSE TE2000-S inverted fluorescence microscope (Japan). The toxicity of HeLa cells was confirmed with Tecan Infinite F50 Microplate

Reader (Germany). All chemicals of analytical grade reagent purchased form Aladdin. Metal ions and anions solution were prepared from the corresponding nitrate salts and sodium salts, respectively. The certified reference materials (CRMS) GBW(E) 081531 (liquid) and (CRMS) GBW(E) 080219 (liquid) were purchased from the National Research Center for Certified Reference Materials (Beijing, China). Tap water sample was got from our lab tap directly. All CRMS and water samples were analyzed without pretreatment. The serum was pretreated by the method that has been reported in the literature [35]. HeLa cells grew on a Cell Culture Flask with Dulbecco's Modified Eagle's Medium, high glucose (H-DMEM) contained 10 % Fetal Bovine Serum (FBS) at 37 ˚C and 5 % CO_2 atmosphere. Double-distilled water was employed in all experiments.

Stock solution (1.00×10^{-4} mol/L) of **QC** was prepared in ethanol as mother samples. Stock solutions (1.00×10^{-3} mol/L) of Cu^{2+}, Mg^{2+}, Ba^{2+}, Cr^{3+}, Zn^{2+}, K^{+}, Bi^{3+}, Ag^{+}, Al^{3+}, Cd^{2+}, Pb^{2+}, Ca^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, Mn^{2+}, Fe^{3+}, Na^{+} and related anions were prepared in double distilled water. The following procedure was employed for the all measurements. To 10 mL volumetric flasks containing different amounts of metal ions, the proper amounts of the solution of **QC** was added directly, then diluted ethanol-aqueous with Hexamethylenetetramine-HCl buffer solutions to 10 mL. After shaking for 10 s and waiting for about 2 min at room temperature, 2-3 mL of the solution was put into the fluorescent or UV-Vis cell and the absorption and fluorescence were run. Fluorescence measurements were carried out with excitation and emission slit width of 5 nm and excitation wavelength was 393 nm. Each value was mean of three replicates.

2.2 Synthesis

2.2.1 Synthesis of quinoline-2-carbonyl chloride (compound 1)

Dichlorosulfoxide (12 mmol, 1.428 g) and pyridine (2.0 mL), in turn, were added drop-wise to quinoline-2-carboxylic acid (12 mmol, 2.067 g) in 30 mL N,N-

dimethyformamide (DMF) at 0 ℃ and under N_2 atmosphere. Then the solution refluxed for 11 h. After removing the solvent under reduced pressure, the crude solid was dried and recrystallized from petroleum to give 1.885 g of white solid of quinoline-2-carbonyl chloride (compound 1) (Scheme 1.). (yield, 82 %; m.p. 97-98 ℃). ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm) 8.55 (d, J = 8.4 Hz, 1H, Ar–H), 8.17 (m, 1H, Ar–H), 8.07-8.02 (2H, Ar–H), 7.97-7.74(m, 1H, Ar–H), 7.72 (t, J = 7.5 Hz, 1H, Ar–H).

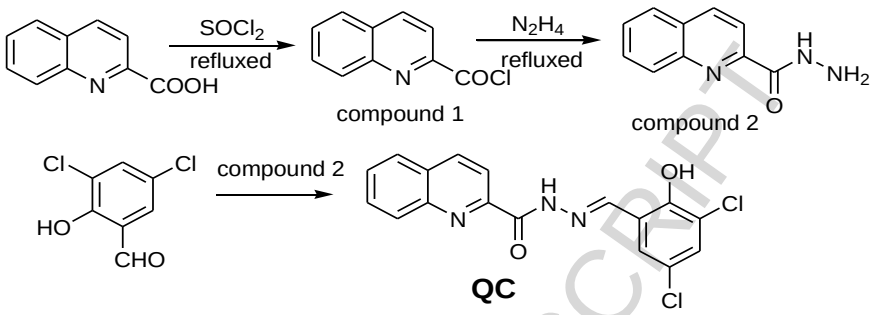
2.2.2 Synthesis of quinoline-2-carboxylic hydrazide (compound 2)

Hydrazine hydrate (10 mmol, 0.412 g) was added to a methanolic solution (50 mL) of quinoline-2-carbonyl chloride (6 mmol, 1.149 g) by droplet. Then the mixture refluxed for 4.5 h. After removing the solvent under reduced pressure, the crude solid was dried and recrystallized from methanol, 0.711 g yellow solid (quinoline-2-carboxylic hydrazide, compound 2) was obtained (Scheme 1.). (yield,63%, m.p. 227–228 ℃).^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm) 9.22 (s, 1H, –NH–), 8.35 (d, J = 8.5 Hz, 1H, Ar–H), 8.28 (d, J = 8.5 Hz, 1H, Ar–H), 8.11 (d, J = 8.5 Hz, 1H, Ar–H), 7.92 (t, J = 10.5 Hz, 1H, Ar–H), 7.65 (t, J = 7.2 Hz, 1H, Ar–H), 7.28 (s, 1H, Ar–H), 4.16 (s, 2H,–NH_2).

2.2.3 Synthesis of QC

A methanolic solution (40 mL) of quinoline-4-carboxylic hydrazide (4 mmol, 0.748 g) was dropped tomethanolic solution (20 mL) of 3,5-dichlorosalicylaldehyde (0.969 g, 5 mmol) and kept the reaction mixture refluxing for 5 h under N_2 atmosphere. After removing the solvent under reduced pressure, the mixture was put into refrigerator for overnight. Then 1.120 g of pale yellow crude solid was obtained by filtration. And the pure **QC** was gotten by silica gel column chromatography (Scheme 1.). (yield, 78%, m.p. 279–280 ℃) IR (KBr disk cm^{-1}): 3309(–NH–), 3078(–OH), 1693, 1448, 1278, 1182(–C–O–C–), 1157, 1143, 771, 732(–C–Cl). 1H NMR (400 MHz, DMSO-d_6) δ(ppm) 12.89 (s, 1H,–NH–), 12.52 (s, 1H,Ar–OH), 8.86 (s, 1H, CH–), 8.61 (d, J = 8.5 Hz, 1H, Ar–H), 8.20 (d, J = 8.5 Hz, 2H, Ar–H), 8.10 (d, J = 7.4 Hz, 1H Ar–H), 7.90

(t, J = 7.2 Hz, 1H, Ar–H), 7.80-7.63 (m, 1H, Ar–H), 7.62 (d, J = 2.4 Hz, 1H, Ar–H), 7.59 (d, J = 2.5 Hz, 1H, Ar–H). Elemental analiysis: $C_{17}H_{11}Cl_2N_2O_2$; Calc., C, 56.69; H, 3.08; N, 11.67; Found, C, 56.72; H, 3.10; N, 11.67. HRMS (MALDI): m/z $(M+1)^+$,359.82.



Scheme 1. The route of synthesis for **QC**.

3. Results and discussion

3.1 Absorption spectra

The absorption spectra of **QC** (10 μM) with Al^{3+} (2.0 equiv.) or other metal ions (2.0 equiv.) were measured in EtOH-H_2O (v/v=1:9, pH=6.0). In the absence of Al^{3+}, the solutions of **QC** produced absorption bands at 313 nm and 340 nm, which could be attributed to a π-π* transition of quinoline, favoured by the planar orientation enforced by the intramolecular hydrogen bonding[36]. Because the intramolecular hydrogen bond was broken after Al^{3+} added, absorption bands at 313 nm and 340 nm red shifted to 330 nm and 393 nm, severally. Furthermore, other ions (including Cu^{2+}, Mg^{2+}, Ba^{2+}, Cr^{3+}, Zn^{2+}, K^+, Bi^{3+}, Ag^+, Cd^{2+}, Pb^{2+}, Ca^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, Mn^{2+}, Fe^{3+} and Na^+) led to no absorption at 393 nm. But the absorption of **QC** with Al^{3+} at 330 nm was influenced by other metal ions (Fig. 1a.). Two legible isosbestic points were obtained at 349 nm and 365 nm, respectively, with increasing the concentration of Al^{3+}, which explicitly implied the formation of **QC**-Al^{3+} and indicated a balanced between **QC** with **QC**-Al^{3+} in solution[37]. Moreover, the absorbance at 393 nm

enhanced gradually with the increasing concentration of Al^{3+} until 1.6 equiv. (Fig. 1b.).

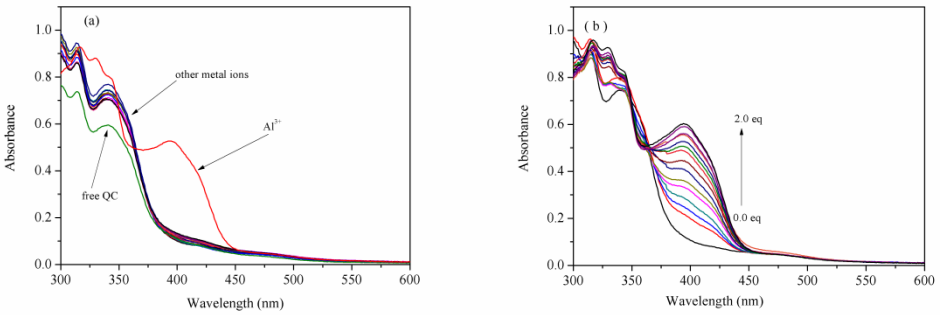


Fig. 1(a). Absorption spectra of **QC** (10 μM, v/v=1:9, pH=6) with different metal ions (20 μM),metal ions including Cu^{2+}, Mg^{2+}, Ba^{2+}, Cr^{3+}, Zn^{2+}, K^{+}, Bi^{3+}, Ag^{+}, Cd^{2+}, Pb^{2+}, Ca^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, Mn^{2+}, Fe^{3+} and Na^{+}. **(b)** Absorbance spectral changes of **QC** (10 μM) up addition of Al^{3+} (0.0-2.0 equiv.).

3.2 Fluorescence spectra

The fluorescence absorption of **QC** (10 μM) with and without Al^{3+} were investigated in EtOH-H_2O (v/v=1:9, λ_{ex}=393 nm) during different pH conditions (Fig. 2.). Without Al^{3+}, the weak fluorescence intensity of **QC** solution could be observed from pH 3.0 to 9.0. Upon addition of Al^{3+} (2.0 equiv.), the fluorescence intensity was dramatically enhanced at pH range from 3.0 to 8.0. Among of them, the fluorescence intensity gradually increased from pH 3.0 to 4.5, attained a plateau from pH 4.5 to 7.0 and then decreased dramatically when the pH values are higher than 8.0. It ascribed that **QC** binding Al^{3+} would be prevented at low pH value and at high pH values, which resulted in weak fluorescence. In the absent of Al^{3+}, there are PET and ESIPT process for free **QC**, which induced by the transfer of the lone pair electrons from nitrogen of –C=N and the formation of a hydrogen-bonding configuration[38] , so the **QC** showed weak fluorescence. But at present of Al^{3+}, Al^{3+} would form a complex with **QC**, which formed effective restraint of the ESIPT and PET process and increased the CHEF process [39] and produced enhancement fluorescence . In current work, pH 6.0 with Hexamethylenetetramine-HCl butter solution was applied to the whole experiment except for cells imaging.

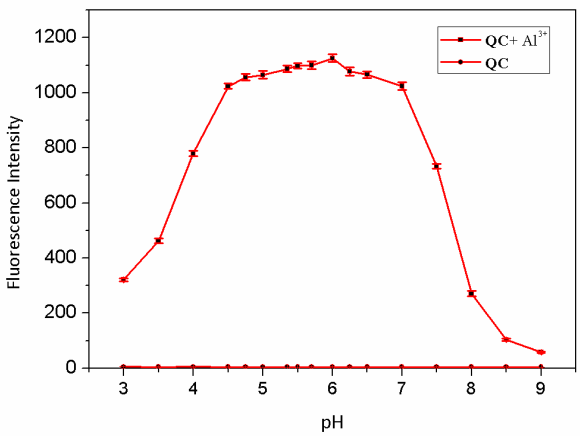


Fig. 2. Variation of fluorescence intensity of **QC** (10 μM) in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm) with and without Al^{3+} (2.0 equiv.) as a function of pH.

Under the same conditions, the fluorescence response of **QC** was performed for 2.0 equiv. Al^{3+} or 2.0 equiv. other metal ions (including Cu^{2+}, Mg^{2+}, Ba^{2+}, Cr^{3+}, Zn^{2+}, K^{+}, Bi^{3+}, Ag^{+}, Cd^{2+}, Pb^{2+}, Ca^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, Mn^{2+}, Fe^{3+} and Na^{+}) (Fig. 3.). It turned out that the fluorescence intensity was obviously enhanced only in the present of Al^{3+} at 493 nm. However, no significant fluorescence changed was observed when other metal ions were added. Furthermore, competition experiments (Fig. 4.), which the solution of Al^{3+} (2.0 equiv.) and other individual cation (10.0 equiv.) were added to probe **QC** (10 μM), were also manifested that the fluorescence intensity of **QC**-Al^{3+} is rarely affected by the other tested metal ions. It ulteriorly proved that the **QC** possess high sensitivity and selectivity to Al^{3+}.

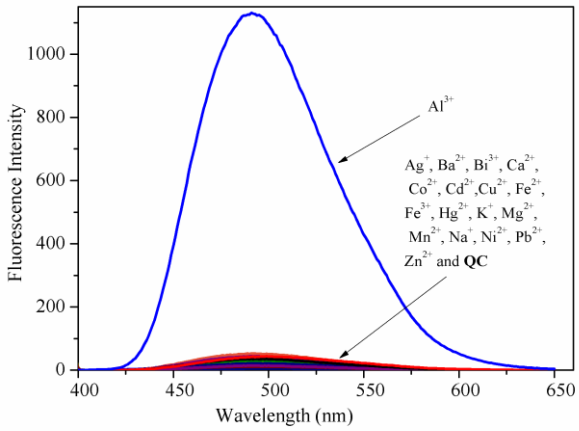


Fig. 3. Fluorescence spectra of **QC** (10 μM) with Al^{3+} (2.0 equiv.)

and various metal ions (2.0 equiv.) in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm).

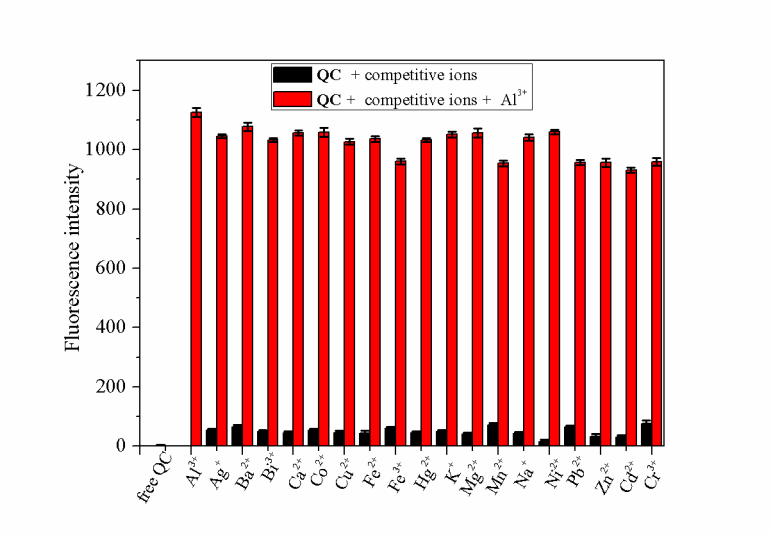


Fig. 4. Selective responses of **QC** (10 μM) for Al^{3+}(2.0 equiv.) in the presence of various competitive metal ions (10.0 equiv.) in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm). Black bars represent the addition of 10.0 equiv. of other metal ions to a 10μM solution of **QC or** free **QC**. Red bars represent fluorescence intensity of a mixture of **QC** (10 μM) with other metal ions (10.0 equiv.) in followed by addition of 2.0 equiv of Al^{3+} to the solution, respectively.

To further study the recognizing abilities of **QC** toward Al^{3+}, fluorescence titrations were carried out. As shown in Fig. 5., the free **QC** (10 μM) emitted weak fluorescence at 493nm in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm). With the gradually increasing concentration of Al^{3+}, the fluorescence intensity at 493 nm continuously enhanced until concentration of Al^{3+} reached 1.6 equiv. As well as, the fluorescence intensity of **QC**-Al^{3+} solution was linear dependence to the concentration of Al^{3+} in the range from 0 μM to 10 μM with the correlation coefficient of R^2=0.9989 (Fig. 5. inset). On the basis of these relationships and 3σ/K, where K was the slope between fluorescence intensity and sample concentration of Al^{3+} at 493 nm, σ was the standard deviation of blank solution, the detection limit was estimated about 0.012 μM (Table 1.). Meanwhile, probe **QC** has water solubility, so it could be applied for water sample and cell imaging. These consequences exhibited that the probe **QC** will play a crucial role in the field of environment monitoring.

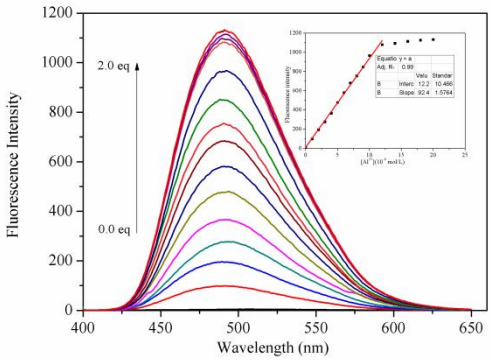


Fig. 5. Fluorescence spectra of **QC** (10 μM) with addition of increasing amount of Al^{3+} (0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 12, 14, 16, 18, and 20 μM) in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm). Inset: fluorescence intensity at 493 nm versus the number of concentration of Al^{3+} added.

Table 1. The comparison of **QC** with some other probes for Al^{3+} ions.

mechanism	Solution (v/v)	LOD(μM)	Application	Reference
FRET	aqueous	0.50	/	[12]
PET	ethanol	0.19	/	[13]
CHEF	DMSO-H_2O 4:6	0.027	/	[21]
PET	ethanol	0.10	/	[22]
PET	ethanol	0.027	/	[23]
FRET	EtOH-H_2O 1:99	0.10	Cell imaging	[39]
PET,CHEF	ethanol	0.082	/	[34]
CHEF	CH_3OH-H_2O 95:5	0.60	/	[40]
ESIPT	DMSO	2.40	Cell imaging	[41]
ESIPT,PET, CHEF	EtOH-H_2O 1:9	0.012	Water samples and Cell imaging	Present work

3.3 Binding mode of QC and Al^{3+}

To investigate the binding mechanism between **QC** and Al^{3+}, the Job's plot for the fluorescence intensity was tested by sustaining the total concentration of 10 μM for **QC** mixed Al^{3+} and altering the mole fraction of Al^{3+} from 0 to 0.9 in EtOH-H_2O (v/v=1:9, pH=6.0) (Fig. 6.). When the molar fraction reached 0.5, the highest fluorescence intensity was obtained, which might informed that the stoichiometric binding mode for **QC**-Al^{3+} was 1:1 in the media [42, 43].

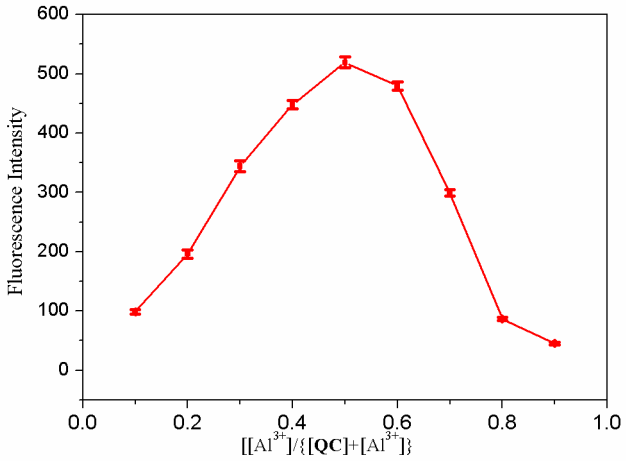


Fig. 6. Job's plot of **QC** with Al^{3+} in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm). Total concentration of **QC** and Al^{3+} was maintained constant at 10μM and the mole fraction of Al^{3+} changed.

Furthermore, the recognition reversibility is a very significant research. The reversibility of complex **QC**-Al^{3+} were investigated through various anion (3.0equiv.), such as I^-, F^-, Br^-, Cl^-, Ac^-, CO_3^{2-}, PO_4^{3-}, S^{2-}, SO_4^{2-}, ClO_4^- and NO_3^- in EtOH-H_2O (v/v=1:9, pH=6.0). As shown in Fig. 7., the results showed that only F^- produced obvious fluorescence quenching at 493 nm, which was ascribed to the F^- reversed the process of the chelation of **QC**-Al^{3+}. The accomplish time of the reversible process was 2 minutes. Fortunately, this cycle process could be repeated multiple times without loss of fluorescence intensity.

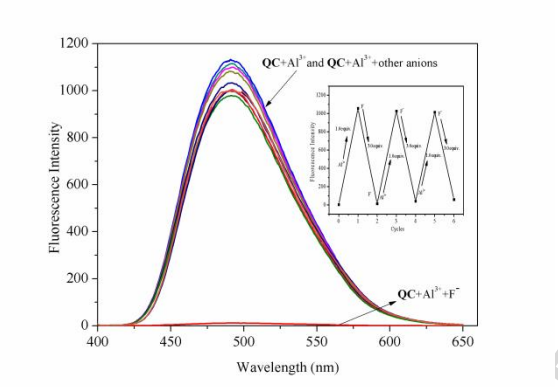


Fig. 7. Fluoresence spectra of **QC**-$Al^{3+}$with different anions (3.0 equiv.).

Anions include I^-, F^-, Br^-, Cl^-, Ac^-, CO_3^{2-}, PO_4^{3-}, S^{2-}, SO_4^{2-}, ClO_4^- and NO_3^-.

Benesi-Hildebrand method was also used to confirm the binding stoichiometry. When hypothesizing a 1:1 associate-ion between **QC** and Al^{3+}, the binding constant was calculated from the fluorescence intensity data according to the Benesi-Hildebrand equations[44, 45]:

$$\frac{F_{max} - F_{min}}{F - F_{min}} = \frac{1}{K_a[Al^{3+}]} + 1$$

F_{min} was the fluorescence intensity of the free **QC**. F was the fluorescence intensity of **QC**-Al^{3+} at any intermediate aluminum concentration. F_{max} was the fluorescence intensities of the complete interaction of **QC** binding aluminum. K_a was the binding constant (M^{-1}) for Al^{3+}**,** [Al^{3+}] represent the concentration of Al^{3+}. The intercept of 1 and the slope of $1/K_a$ would be expected in a regression plot of $(F_{max} - F_{min})/(F - F_{min})$ vs. $1/[Al^{3+}]$. As the plot of titration profiles showed, excellent linearity was exhibited 1:1 binding mode between **QC** and Al^{3+} (Fig. 8.), and K_a was calculated as 8.44×10^4 M^{-1} based on slope and intercept.

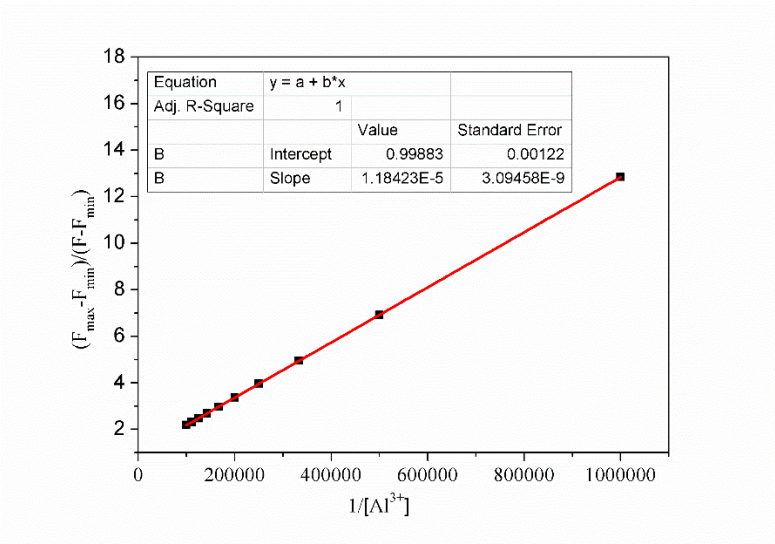
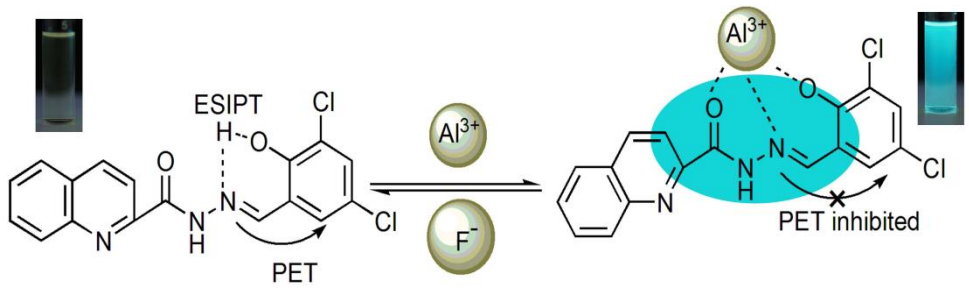


Fig. 8. Benesi-Hildebrand plot of **QC** (10 μM) at different concentration Al^{3+} (0-10 μM) in EtOH-H_2O (v/v=1:9, pH=6, λ_{ex}=393 nm).

To further define the bonding formation of **QC**-Al^{3+}, the ^{1}H NMR titration experiments were executed with or without Al^{3+} in DMSO-d_6. In ^{1}H-NMR titration, Al^{3+} was put into the DMSO-d_6 solution of **QC** and spectral change was obtained (Fig. S_1, Supporting information). These peaks at 12.89 ppm and 12.52 ppm should respectively represent the labile protons of –NH– and –OH. The proton peak of the –OH at 12.52 ppm vanished and the proton signal of the imine (–NH–) at 12.89 ppm slightly receded while Al^{3+} existed. When 3.0 equiv. of F^- was added, the peak of –OH at 12.52 ppm and –NH– at 12.89 ppm were recovered. These results might informed that **QC** may chelate Al^{3+} by interaction with oxygen atoms from –C=O and –OH of the salicylaldehyde hydroxyl group and nitrogen atom of –C=N [17, 46] (Scheme 2.). Namely, the change of **QC** fluorescence intensity in the case of Al^{3+} ion was owed to the formation of **QC**-Al^{3+} complex through two oxygen of carboxylate and phenol groups respectively, and nitrogen of imine moiety with Al^{3+}, which formed effective restraint of the ESIPT and PET process and increased the CHEF process[33].



Scheme 2. Proposed mechanism for detection of Al^{3+} and F^- by **QC**

3.5 The preliminary application of QC

To verify the accuracy of the fluorescence spectra method for **QC** detect Al^{3+}, two certified reference materials (CRMs)(GBW(E)081531 GBW(E)080219) were used. These analytical results matched the standard values of CRMs (Table 2.). It was easy to see from Table 2., these values (error rates 5%) of $T_{measurement}$ were smaller than the corresponding $T_{references}$ values[47], which indicated fluorescence spectra method is reliable. Furthermore, to evaluate unknown concentration of Al^{3+} in the real samples, standard addition method was used with $Al(NO_3)_3$ (GBW(E) 080219) as standard material (Table 3.). The results showed that the concentrations of Al^{3+} were found to be 0.25 ± 0.033 μM and 2.10 ± 0.11 μM in the volunteer serum and dialysis patient serum, respectively, which were consistent with the reference[48] , and 2.86 ± 0.033 μM in the tap water. At the same time, the recovery rates of Al^{3+} were in the range of 98.6%–102.3%. So, the provided detection method for Al^{3+} possesses high accuracy and precision.

Table 2. Analytical results for the detection of Al^{3+} in certified reference materials.

Sample	Concentration of Al^{3+}(μg/mL)		T-test	
	Certified	Measured	$T_{(references)}$[47]	$T_{(measurement)}$
GBW(E) 081531	100	99.983	4.303	0.536
GBW(E) 080219	100	99.9962	4.303	1.068

Table 3. Analytical results for the detection of Al^{3+} in serum and tap water samples.

Sample	Concentration of Al^{3+}(μM/L)		Recovery Rate(%)
	Added of $Al(NO)_3$	Measured	
Volunteer serum	0.00	0.25±0. 021	0.0
	2.00	2.22±0.045	99.5
	4.00	4.24±0.034	101.2
	6.00	6.25±0.010	98.6
dialysis patient serum	0.00	2.20±0.12	0.0
	2.00	4.19±0.15	99.6
	4.00	6.21±0.09	102.3
	6.00	8.21±0.10	98.9
tap water	0.00	2.86±0.015	0.0
	2.00	4.85±0.035	100.7
	4.00	6.91±0.027	101.3
	6.00	8.90±0.056	98.9

3.6 Cell studies of QC in the presence of Al^{3+}

To test the cytotoxicity of probe **QC** and Al^{3+}, these HeLa cells were incubated with different concentration of probe **QC** (0 to 60 μM) and Al^{3+} (1 μM – 100 μM). Then cell viability was determined by an MTT assay. As shown in Fig. 9., these results represented no toxicity to HeLa cells in the present of 0-10 μM **QC** and 1-10 μM Al^{3+}.

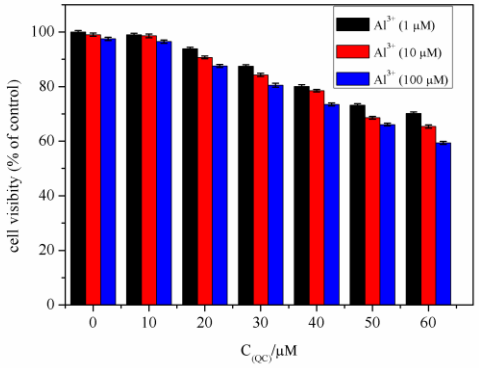


Fig. 9. The cytotoxity of **QC** in HeLa cells.

Subsequent experiments were aimed to evaluate whether **QC** could be used to fluorescently visualize Al^{3+} in living matrices. Hela cell were first incubated with 10 μM solution of probe **QC** for 30 min at 37 °C and washed twice with PBS. Finally, Hela cells (or the treated cells) exposed to 10 μM solution of Al^{3+} for another 30 min at 37 °C and washed with H-DMEM before imaging. As shown in the Fig. 10., no intracellular fluorescence (Fig. 10a., 10b.) was observed when the cells were only treated with solution of **QC**. While strong fluorescence (Fig. 10e.) was observed in cells exposed to **QC** and Al^{3+}. Cells that were exposed to Al^{3+} did not displayed fluorescence (data not shown). And the bright-field transmission image of cells treated with **QC** or Al^{3+} (Fig. 10a. and d.) confirmed that the cells were viable throughout the imaging experiments. These results indicated that probe **QC** was cell permeable and may be used to detect Al^{3+} in biological sample.

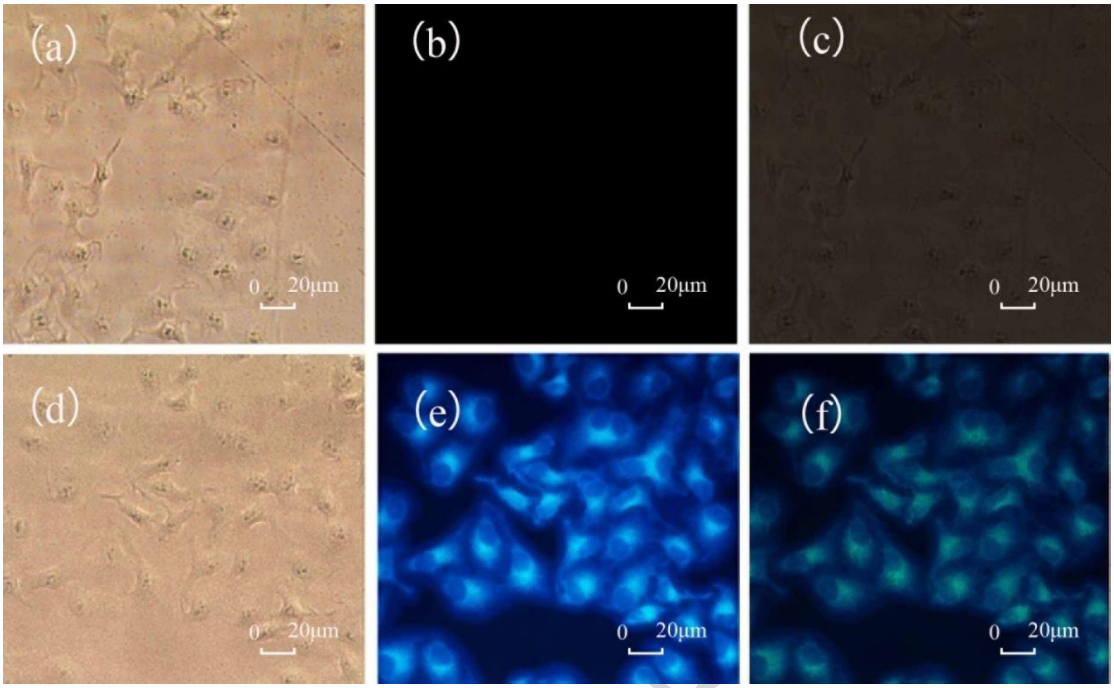


Fig. 10. Bright field (a) and fluorescence image (b) of HeLa cells (40X) incubated with probe **QC** (10 μM) for 30 min; Bright field (d) and fluorescence image (e) of HeLa cells (40X) incubated with probe **QC** (10 μM) and Al^{3+} (10 μM) for 30 min. Fluorescence image taken from (b & e) green channel (480 nm -530 nm). (c) overlay image of (a) - (b); (f) overlay image of (d) - (e).

4. Conclusions

In a word, a novel turn on fluorescence probe **QC** based on quinoline has been developed, which showed high selectivity and sensitivity in the present of concomitant metal ions (including: Cu^{2+}, Mg^{2+}, Ba^{2+}, Cr^{3+}, Zn^{2+}, K^{+}, Bi^{3+}, Ag^{+}, Cd^{2+}, Pb^{2+}, Ca^{2+}, Hg^{2+}, Co^{2+}, Ni^{2+}, Fe^{2+}, Mn^{2+}, Fe^{3+} and Na^{+}) via a 1:1 binding mode with the binding constant being $8.44 \times 10^{4}\ M^{-1}$ in EtOH-H_2O (v/v=1:9, pH=6). And F^{-} can reverse the fluorescence of **QC**-Al^{3+}, which would be used to test F^{-} in the same system. In addition, the interaction mechanism of **QC** and Al^{3+} was proposed. An effective fluorescence analysis method for Al^{3+} has been set up with the concentration of Al^{3+} in the range of 0-10 μM, and the detection limit was found to be 0.012 μM. Finally, the probe **QC** indicated the worth for test of intracellular Al^{3+}. Therefore, the probe **QC** displays strong potential for applications in environmental monitoring and biological diagnostics analysis.

Acknowledgments

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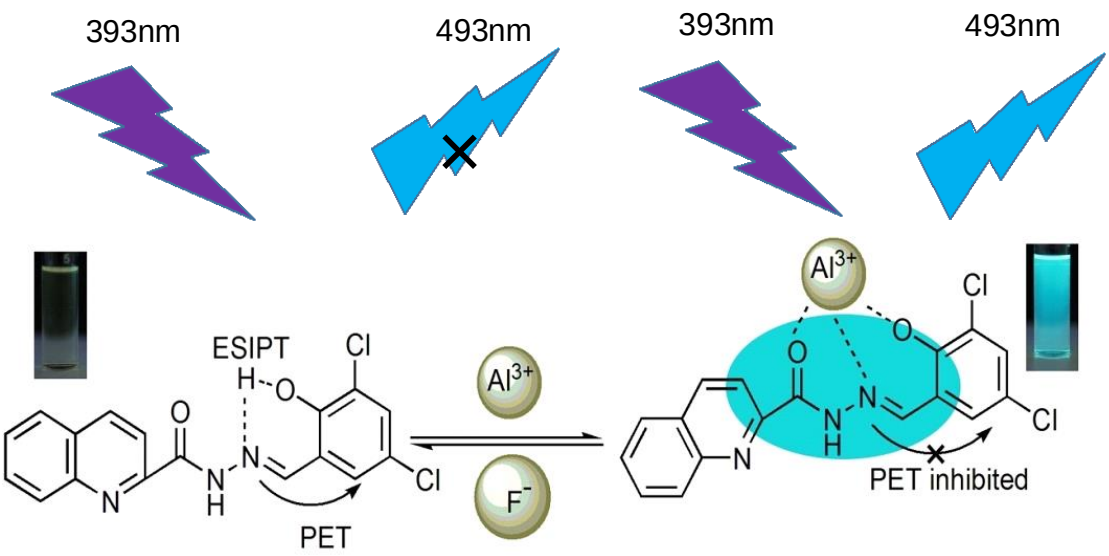

Graphical abstract

Highlights

1) A novel turn on fluorescent probe for aluminum(III) based on asymmetric quinoline Schiff's base has been synthesized.

2) The fluorescent probe **QC,** which could apply in water sample, serum and cell image, has higher selectivity and lower limit of detection for Al^{3+} comparing with the previous reports.

3) Binding mode and coordination sites of probe **QC** with Al^{3+} were proposed.

4) The rate of water in the solvent was increased.