1

Quinoline-Based Fluorescence Sensors

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1. Introduction

The human body is full of various ions, which play an important role in the normal physiological activities. For example, Zinc ion (Zn^{2+}) plays a vital role in protein organism and in many biochemical processes, such as inducing apotosis, enzyme regulation, and gene expression. Also, Ferrous ion (Fe^{2+}) is vital in the oxygen transporting. But there are some ions harmful to human body. When exposed to mercury, even at a very low concentration, they lead to kidney and neurological diseases. What's more, Cadmium (Cd^{2+}) could damage our tissues, resulting in renal dysfunction or even cancers. So far, we have known more about these ions' properties in metabolism, but little is known on mechanism.

We need a forceful instrument to study these mechanisms, need to know when and where ions are distributed, when ions are released, and so on.Therefore, traditional methods such as titration and electrochemistry are obviously unsuitable for in vivo detection. As a result, to accomplish the job, we need new tools and methods, among which fluorescence sensors are a good choice. So, what is a sensor? "Sensor" is a very broad concept, which accepts physical or chemical variables (input variables) information, and converts them into the same species of other kinds or converts their nature of the device output signal (Fig. 1) by following certain rules.

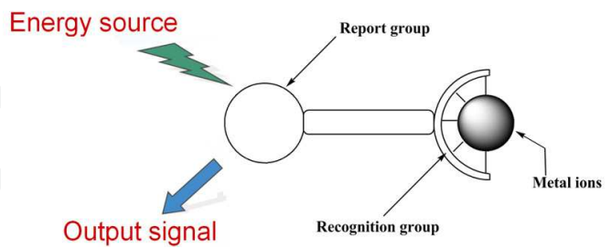


Fig. 1. Sensor structure (Once combination of ions, the output signal will change)

A chemosensor or a molecular sensor is a molecule that interacts with an analyte to produce a detectable change. Chemosenors consist of receptor and reporter, and after the receptor binds with a guest, the signal observed by the reporter will change. Fluorescent sensor is one of the most important chemosensors which uses fluorescence as the output signal, and also a powerful tool to monitor the metal ions in vivo system because of its simplicity, high sensitivity and real-time in situ imaging. In recent years, more and more chemosensors, especially the fluorescent sensors have been used to detect different ions, elbowing their

way to center stage in the field of molecular recognition. Series of sensors based on fluorescein, coumarin, petide, quinoline, and proteins have been used to detect intracellular ions concentration, such as Zn^{2+} sensors of Zinpyr Family based on fluorescein designed by Woodroofe (2004) et al., Cadmium sensor based on boradiazaindacene synthesised by Xu (2007) et al., Cu^{2+} sensor based on rhodamine synthesised by Dujols (1997) et al., the benzimidazole sensor described by Henary (2004) et al., the protein sensor described by van Dongen (2006) et al., Hg^{2+} FRET sensor described by Joshi (2010) et al., and Fe^{3+} sensor based on 1,8-diacridylnaphthalene and synthesized by Wolf (2004) et al..

Different fluorophores bring different optic properties of sensors. For example, sensors based on rhodamine can be excited by visible light, but they get low Stock's shift. Benzofuran-based sensors get lower dissociation constant, but UV exiting with higher energy may damage cells. These disadvantages thus bring forward potential difficulties for quantitative determination and bioimaging, so how to solve these problems is still a challenge.

Quinoline sensors, especially Zn^{2+} and Cd^{2+}, have high selectivity and low detection limit (nM or pM). Modified quinoline chemosensors can also use low energy two-photon laser as the exciting source, which can reduce cell damage. Therefore, the current research of quinoline-based sensors attracts more and more attention.

Herein, the mechanism of quinoline-based fluorescence sensing, including PET (Photoinduced electron transfer), ICT (intermolecular charge transfer) and FRET (fluorescence resonance energy transfer), the synthetic strategies for functionalization of quinoline-based sensors will be reviewed, and the reasons for the choice of a particular synthetic pathway will be discussed. In order to contextualize the potential applications, a brief introduction of the photophysics property concerning quinoline-based sesnors is contained in the essay. At the same time, calculation method of sensor properties (eg, dissociation constant and quantum yield determination) is also included.

2. Mechanism of quinoline-based fluorescence sensing

Quinoline-based fluorescence sensors are usually used to measure intensity changes of fluorescence and/or shift of fluorescence wavelength. Photoinduced electron transfer (PET), intermolecular charge transfer (ICT) and fluorescence resonance energy transfer (FRET) are the three major mechanisms of fluorescence signal transduction in the design of quinoline-based fluorescence chemosensors (de Silva (1997) et al., Sarkar (2006) et al. and Banthia & Samanta (2006)). We will present the basic concepts of these mechanisms.

Chemosensors based on PET mechanism (Fig. 2) often use a atoms spacer less than three carbon atoms to connect a fluorescence group to a receptor containing a high-energy non-bonding electron pair, such as nitrogen or sulfur atom, which can transfer an electron to excited fluorescence group and result in fluorescence quench. But when the electron pair is coordinated by a metal ion (or other cation), the electron transfer will be prevented and the fluorescence is switched on. Most of quinoline-based fluorescence enhancement sensors can be explained by the PET type. Generally speaking, wavelengths of most PET chemosensors in Stokes shifts are less than 25 nm, which produces potential difficulties for quantitative determination and bioimaging. However, ratiometric chemosensors, which observe changes

in the intensity ratio of the two wave bands in absorption and/or emission, would be more favorable in increasing the signal selectivity and can be widely used in vivo.

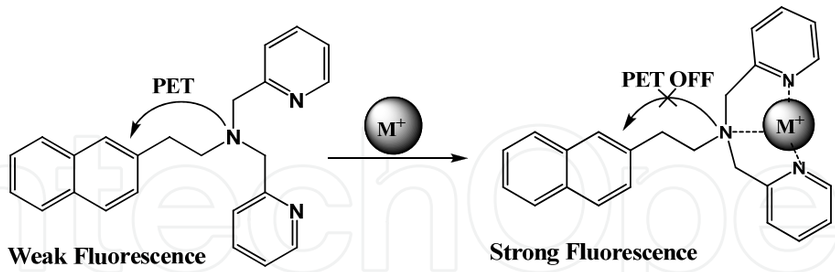


Fig. 2. PET mechanism (The intensity of Fluorescence will increase after combination of ions)

The ICT mechanism (Fig. 3) has been widely used in the design of ratiometric fluorescent chemosensors. Compared to PET mechanism, this type of chemosensor doesn't have any spacer. If a receptor (usually an amino group) is directly connected with a conjugation system and forms a new conjugation system with p-electron, resulting in electron rich and electron poor terminals, then ICT from the electron donor to receptor would be enhanced upon light excitation. When a receptor, as an electron donor within the fluorophore, is bound with a metal ion (or another cation), the cation will reduce the electrondonating capacity of the receptor and a blue shift of the emission spectrum is obtained. In the same way, if a receptor is an electron receptor, the coordination of the cation will further strengthen the push – pull effect. Then a red shift in emission will be observed. For example, the coordination of Zn^{2+} with quinoline derivatives can induce a red-shift ratiometric fluorescence signal.

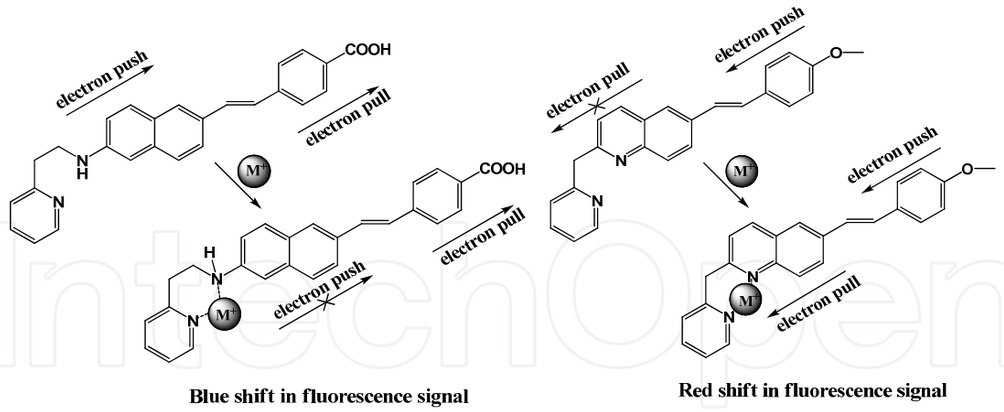


Fig. 3. ICT mechanism (Change in the intensity ratio of the two wave bands in emission)

Recently, the fluorescence resonance energy transfer (FRET Fig. 4), which involves the nonradiative transfer of excitation energy from an excited donor to a proximal ground-state acceptor, has been employed to design ratiometric sensors. The FRET-based sensors can be designed in the form of a small molecule, which usually contains two fluorophores connected by a spacer through covalent links. The following conditions must be satisfied for FRET: 1. The donor probe should have sufficient lifetime for energy transfer to occur. 2. The distance from the donor to the acceptor must be less than 10nm. 3. The absorption spectrum

of the acceptor fluorophore must overlap with the fluorescence emission spectrum of the donor fluorophore (by approximately 30%). 4. For energy transfer, the donor and acceptor dipole orientations must be approximately parallel. Energy transfer is demonstrated by quenching of donor fluorescence with a reduction in the fluorescence lifetime, and an increase in acceptor fluorescence emission. FRET is very sensitive to the distance between fluorophores and can be used to estimate intermolecular distances. FLIM imaging can be used in association with FRET studies to identify and characterize energy transfer. Quinoline comprising another fluorophore (usually rhodamine) that will behave as FRET donor has been synthesized in order to produce FRET-based chemosensors.

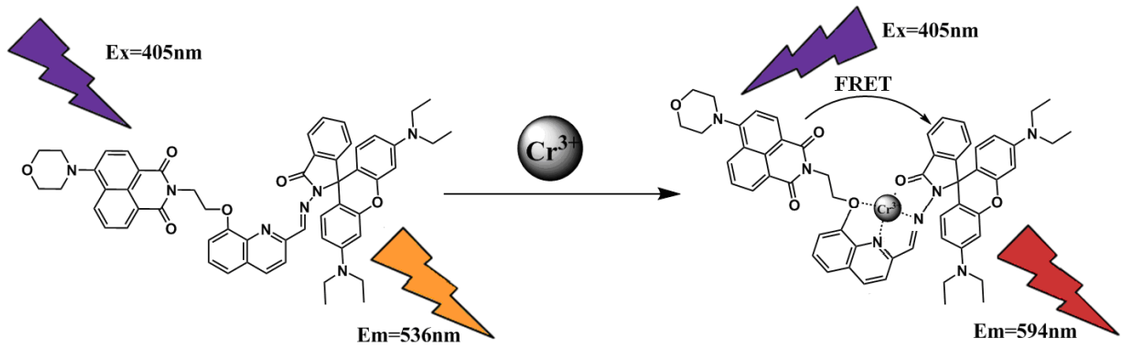


Fig. 4. A FRET chemosensor reported by Zhou (2008) et al.

It is worth mentioning that the combination of PET and ICT mechanisms in the design of chemosensors would be valuable, since a wavelength shift and fluorescence intensity enhancement can amplify the recognition event to a greater extent, for example, using decorated quinoline as mother nucleus, thus oxidizing methyl on 2 position, then connecting DPA group. Thereby excellent ICT effect and fluorescent shift can be obtained after nitrogen atom on quinoline is bound. Meanwhile, the binding N-atom on DPA can obstruct PET process, thus increasing fluorescent intensity. FRET process is also considerably flexible, which can be applied widely in double fluorescence group, and at the same time can be employed in the energy transfer between a single fluorescence group and nanoparticles. By using specific acceptor to separate fluorescent group from nanoparticles, FRET process will be blocked, and fluorescence is produced. By using acceptor to connect nanoparticles with fluorescent group, which was not formerly connected with nanoparticles, fluorescence vanishes. They are particularly significant to fluorescent sensors based on nanoparticles. These methods are extremely effective.

3. Structure and synthesis

The general structure of quinoline-based chemosensors is represented in Fig 5. Most quinoline-based sensors change the receptor group in the 2 (R_1) and 8 (R_5) positions, and the electron donating or withdrawing group in the 4 (R_2), 5 (R_3) and 6 (R_4) positions. Depending on the substituents R_1, R_2, R_3, R_4, R_5, the sensor will present different photophysical properties in solution, such as absorption and emission maxima (λ_{max} abs, λ_{max} em, and fluorescence quantum yield). Herein, the synthesis of different functionalized quinoline-based sensors will be discussed.

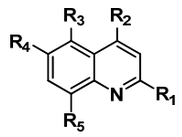
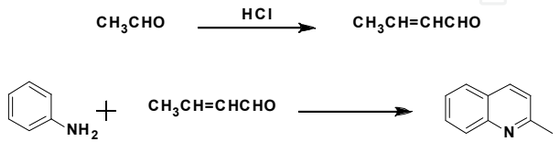


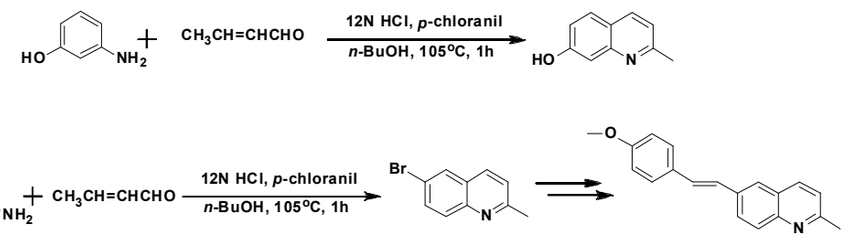
Fig. 5. Molecular structure of quinoline-based chemosensors.

Synthesis by Doebner-Von Miller (1996): According to this method, aniline and acetaldehyde are usually used as raw material in hydrochloric acid or zinc chloride. At the beginning, condensation acetaldehyde into crotonaldehyde, then crotonaldehyde reacts with aniline molecule, the intermediate product is produced, and then dehydrogenates into dihydroquinoline, which becomes 2-methylquinoline. The reaction formula is as follows:



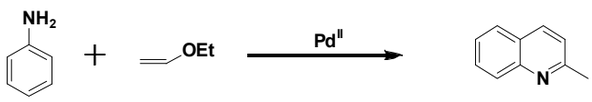
(1)

The improved method, which can also be applied to obtain larger conjugated system in other materials, uses crotonic aldehyde instead of methanal to get a higher yield. In this project, a sensor based on ICT and FRET mechanisms is designed and synthesized, which uses 4-bromo-phenylamine as raw materials. Besides, 4-methoxy styrene is introduced into the quinoline platform by applying the classic Heck reaction.



(2)

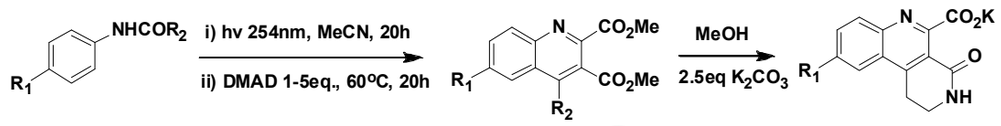
Matsubara (2011) et al. reported a new synthesis method of functionalized alkyl quinolines, which was based on sequential $PdCl_2$-catalyzed cyclization reactions of substituted anilines and alkenyl ethers. High efficiency and functional-group tolerance made this procedure widely applied in synthesis of a number of substituted 2-alkylquinolines and larger conjugated systems.



(3)

Guerrini (2011) group reported an innovative and convenient synthetic approach for synthesizing two important genres of heterocyclic scaffolds, which use the capability of the

aromatic amides to rearrange photo-Fries. Quinolines from simple acetanilides derivatives have been obtained with satisfactory yield by using a single one-pot procedure.



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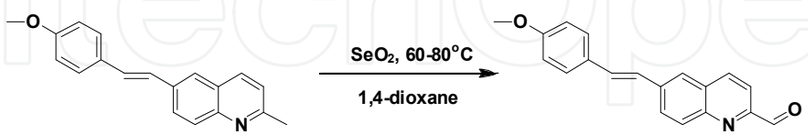
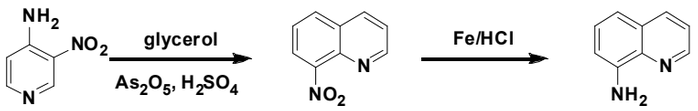


(5)

In order to introduce functional groups on the 2-position, we often oxidize the methyl to aldehyde. Using selenium dioxide as oxidant can gain very high yield. Generally dioxane is used as the reaction solvent at 60-80 degrees. Reaction usually ends within two hours.

The synthesis of 8-aminoquinoline: The cyclization reaction can be firstly adopted to synthesize quinoline, which is replaced by nitryl and its derivatives, then reduction is used to generate 8-aminoquinoline. Classic reactions to synthesize quinoline ring include Friedlander, Skraup, Dobner-Miller and so on. The reaction equation is as follows:



(6)

4. Dissociation constant and quantum yield determination

The dissociation constant is commonly used to describe the degree of affinity between sensor and metal ion. It is a key parameter used to describe the sensor's selectivity. It can be calculated by eq 1,

$$Kd = \frac{[M^{n+}]_{free}(F\max - F)}{F - F0} \tag{1}$$

where F=normalized fluorescence intensity, K_d=dissociation constant, F_{min}=fluorescence intensity without metal ions (M^{n+}), F_{max}=fluorescence intensity of bound sensor and $[M^{n+}]_{free}$ is the concentration of the free M^{n+}. Free metal ion concentrations are controlled by metal ion buffers (e.g., NTA (nitrilotriacetic acid), EDTA or other chelating agent.). As for log K of different metals with NTA and EDTA, see Tab. 1 (log K (ML), I=0.1mol/L, 25°C, 0.1mol/L).

Quinine sulfate is widely used as the standard in the calculation of fluorescence quantum yields of quinoline-based chemosensors (in 0.1N H_2SO_4, Φ =0.55, λ_{ex} = 320 nm). The quantum yields are calculated by eq 2.

$$\Phi U = \frac{\Phi S(FuAs)}{FsAu} \quad (2)$$

A_u is the UV absorption of unbound sensor or bound sensor, with A_s being the standard. F_u is integrated fluorescence emission corresponding to sensor or metal complex, and F_s is the standard.

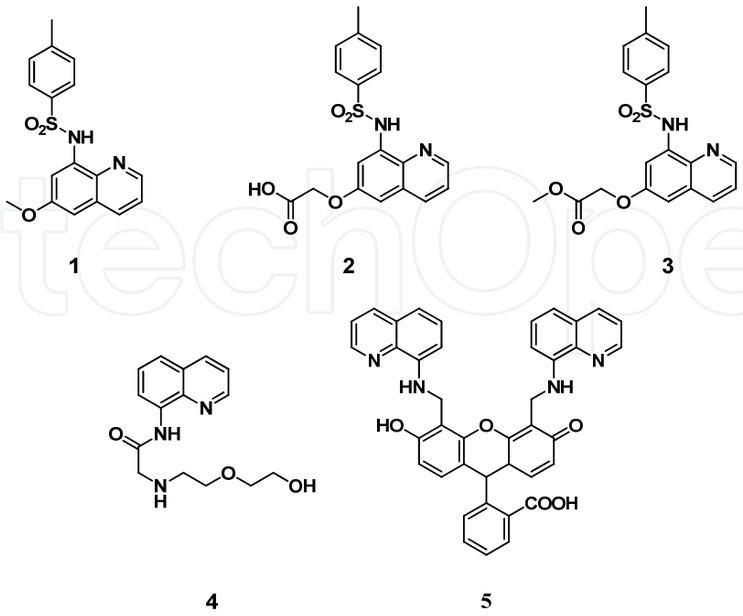
	Ca^{2+}	Cd^{2+}	Zn^{2+}	Co^{2+}	Cu^{2+}	Fe^{3+}	Hg^{2+}	Pb^{2+}	Mg^{2+}
EDTA	10.61	16.36	16.44	16.26	18.70	25.0	21.5	17.88	8.83
NTA	6.39	9.78	10.66	10.38	12.94	15.9	14.6	11.34	5.47

Table 1. Log K of different metals with NTA and EDTA.

5. Quinoline used for detecting different metal ions

5.1 Quinoline used for detecting Zn^{2+} ion

Quinoline and its derivatives, especially 8-hydroxyquinoline and 8-aminoquinoline, are very important fluorogenic chelators for metal ions transition. Derivative of 8-aminoquinoline with an aryl sulfonamide is the first and most widely applied fluorescent chemosensor for imaging Zn^{2+} in biological samples. It was first reported by Toroptsev and Eshchenko. In 1987, Frederickson (1987) et al. reported a new quinoline-based sensor 1, which showed 100 folds in fluorescence enhancement after being bound with Zn^{2+}. And it is the first high-sensitive sensor to detect Zn^{2+} in high concentrations of Ca^{2+} and Mg^{2+}, which is very important for application in vivo. But low water solubility limits its application, so Zalewski (1994) led in a water-soluble group at the 6-position of quinoline, chemosensors 2 and 3 were synthesized. The research showed that this improvement made these two chemosensors much more water-soluble, and also showed a large increase in fluorescence upon Zn^{2+}addition. Ca^{2+} and Mg^{2+} had little effect on the fluorescence whereas Fe^{2+} and Cu^{2+} quenched the fluorescence. Recently, Zhang (2008) et al. reported a new high-selective water-soluble and ratiometric chemosensor 4, based on 8-aminoquinoline for Zn^{2+} ion, which showed 8-fold increase in fluorescence quantum yield and a 75 nm red-shift fluorescence emission from 440 to 515 nm. But its excited source's energy is too high to be applied in vivo. Except the ability to be the fluorescence report group, quinoline's capability of binding Zn^{2+} enables it to be used as merely a binding group, so that high selectivity recognition of Zinc ion can be achieved. Nolan and Lippard (2005) et at., use ethyl 8-aminoquinoline to synthesize chemosensor 5. In addition, 5 exhibits 150-fold increase in fluorescence upon Zn^{2+} binding because of the low background fluorescence and high emission when binding with Zn^{2+}. This binding is selective for Zn^{2+} from other biologically relevant metal cations, toxic heavy metals, and most first-row transition metals and is of appropriate affinity (K_d=41uM) to reversibly bound Zn^{2+} at physiological levels, and the quantum yield for the Zn^{2+}-bound complex is 0.7 (λ_{ex}=518nm). In this job, quinoline's recognition of Zinc ions is utilized. Meanwhile, rhodamine's high yield of fluorescent quantum and high sensitivity are taken full advantage of. So we can see that excellent properties such as light excitation provide superior possible ways for designing quinoline sensors.



8-Hydroxyquinoline, also a traditional fluorogenic agent for analyzing Zn^{2+} and other metal ions, was used as a reporter group in the chemosensor. Di-2-picolylamine (DPA) is a classic chelator with high selectivity for Zn^{2+} over other metal ions that can not be influenced by higher concentration of Ca^{2+}, Na^{+} and K^{+} ions in biological samples. Xue (2008) et al. incorporated DPA into 8-hydroxy-2-methylquinoline at the 2-position to prepare a series of chemosensors 6, 7 and 8. The NMR studies and crystal structures of Sensor–Zn^{2+} complexes indicated that oxygen at the 8-position participated in the coordination of Zn^{2+} along with the quinoline nitrogen atom, and that DPA group endow the sensor with a high affinity (7, K_d = 0.85 pM). The fluorescence intensities of sensors showed a 4 to 6 fold enhancement and the quantum yields were also remarkably enhanced (Fig. 6a). According to the study of sensor's selectivity, the emissions of sensors showed slight enhancement upon addition of K^{+}, Mg^{2+} and Ca^{2+} in the millimolar range, whereas the fluorescence intensities were slightly quenched by 1 equiv. of transition metals such as Mn^{2+}, Co^{2+}, Fe^{2+}, Ni^{2+} and Cu^{2+}, with the exception of Cd^{2+} showing enhanced fluorescence. Xue (2009) improved the sensor via choosing ICT process instead of PET process. By adding a cation which interacted with a receptor, the electron-withdrawing ability of the expanded conjugated system was enhanced, and 8 was designed. This results in a larger red-shift emission and Stokes shift (Fig. 6b). 8 shows a maximum emission at 545 nm with a large Stokes shift of 199 nm in the absence of Zn^{2+}. The ratio of emission intensity (I_{620} nm/I_{540} nm) increases linearly with increased Zn^{2+} concentration. Ratiometric has brought about higher sensitivity, and other background disturbance. Only Zn^{2+} and Cd^{2+} show distinct ratiometric responses. Cell staining experiments demonstrate that 8 can readily reveal changes in intracellular Zn^{2+}. Dual emissions and cell-permeable nature of 8 make it possible to study cellular Zn^{2+} in hippocampus in a ratiometric approach. The same problem appears here too: high-energy excitation puts cells vulnerable to harm.

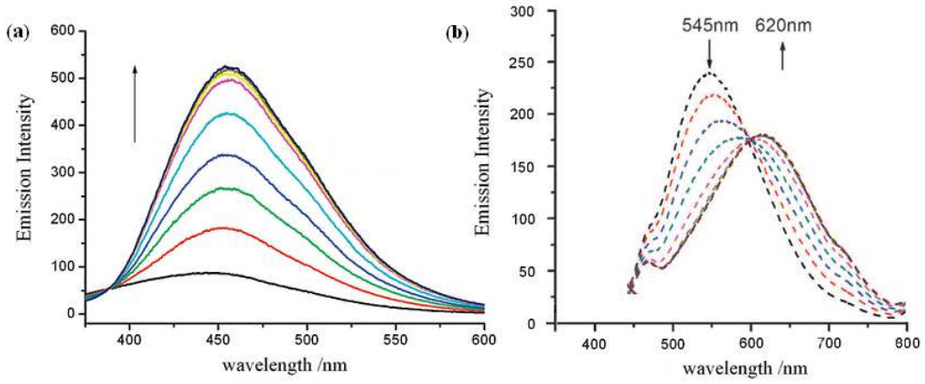
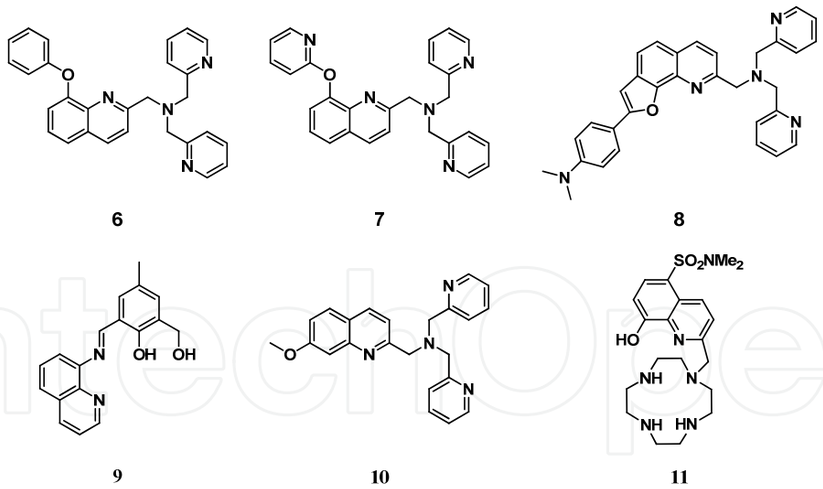


Fig. 6. (a) Fluorescence spectra (λ_{ex}=320 nm) of 5μM 6 upon the titration of Zn^{2+} (0–1.6 equiv.) in a HEPES buffer. (b) Fluorescence response upon titration of 8 (5 mM) with Zn^{2+} (0–1.6 equiv.), λ_{ex}=405 nm.

One year later, a both visual and fluorescent sensor 9 for Zn^{2+} was synthesized by Zhou (2010) et al., it displays high selectivity for Zn^{2+} and can be used as a ratiometric Zn^{2+} fluorescent sensor under visible light excitation. The strong coordination ability of Zn^{2+} with 9 leads to approximately 14-fold Zn^{2+} enhancement in fluorescence response and more than 7-fold increase in quantum yield (form 0.006 to 0.045) in THF-H_2O solution. It is important that 9 have little or no effect on Cd^{2+}, whereas Cu^{2+} and Co^{2+} quench the fluorescence. The quenching is not due to the heavy-atom effect, for, other heavy-atom did not quench the fluorescence.



In recent years, two-photon microscopy (TPM) imaging has gained much interest in biology because this method leads to less phototoxity, better three dimensional spatial localization, and greater penetration into scattering or absorbing tissues. Sensor 10 for monitoring Zn^{2+} was synthesized by Chen (2009) et al. based on the structure of 7-hydroxyquinoline. Its fluorescence enhancement (14-fold) and nanomolar range sensitivity (K_d=0.117 nM) were favorable in biological applications. JOB'S plot, NMR study and X-ray crystal structure indicated the binding model between sensor and Zn^{2+} is 1:1. Moreover, 10 also showed high selectivity for Zn^{2+} toward other first row transition metal ions including Fe^{2+}, Co^{2+}, and

Cu^{2+}, but it was slightly enhanced by Cd^{2+}. Furthermore, 10 can be used for imaging Zn^{2+} in living cells with two-photon microscopy (Fig. 7). This is also one of the directions of designing fluorescence sensors, that is, using widely used low-energy 800nm laser as excitation source so as to avoid the harm to cells caused by ultraviolet rays.

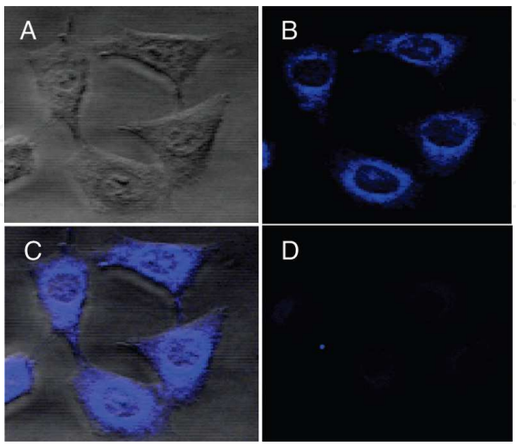
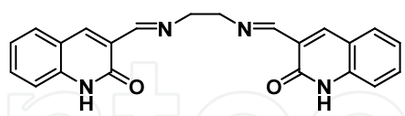


Fig. 7. (A) Bright-field image of A431 cells labeled with 30 μM 10 after 30 min of incubation, λ_{ex}=800 nm. (B) TP image after a 30 min treatment with zinc(II)/pyrithione (50 μM, 1:1 ratio). (C) The overlay of (A) and (B). (D) TP image of cells that are further incubated with 50 μM TPEN for 10 min.

Aoki, S. (2006) et al. have designed and synthesized new cyclen-based Zn^{2+} chemosensor 11 having an 8-hydroxy-5-N and N-dimethylaminosulfonylquinoline unit on the side chain. In the study, they found that using deprotonation of the hydroxyl group of 8-HQ and chelation to Zn^{2+} at neutral pH allows more sensitive detection of Zn^{2+} than dansylamide-pendant cyclen and (anthrylmethylamino) ethyl cyclen. They also introduced deprotonation behavior and fluorescence behavior, which was different by modifying the 5-position. This was very important in designing Quinoline-based chemosensors.



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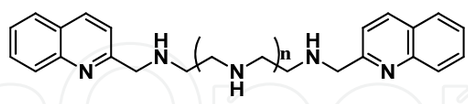


13 n=0,1,2

A space comprised of nitrogen atoms with quinoline fragments at both ends is often used in detection of Zn^{2+}. Sensor 12 was synthesized by Liu (2010) et al, by using ethidene diamine to connect two 2-oxo-quinoline-3-carbaldehydes, thus schiff-base was composed to achieve Zn^{2+} detection. Compared with other metal ions, chemosensor 12 exhibits high selectivity and sensitivity for Zn^{2+} in acetonitrile solution compared with Cd^{2+} and other metal ions (Fig. 8a). The single crystal was taken for demonstrating the binding model of sensor and Zn^{2+}. A simple-structured sensor 13 was reported by Shiraishi (2007) et al. 13 was easily synthesized by one-pot reaction in ethanol via condensation of diethylenetriamine and 2-quinolinecarbaldehyde followed by reduction with $NaBH_4$. 13 is a new member of the water-soluble fluorescent Zn^{2+} sensor capable of showing linear and stoichiometrical response to Zn^{2+} amount without background fluorescence. 13 also shows high Zn^{2+}

selectivity and sensitivity in water solution (Fig. 8b). Cd^{2+} induces slight enhancement of fluorescence emission intensity. It is a easily synthesized recognition to connect two 2-position quinoline sensors through a bridge that comprises heteroatoms (usually N, O, S atoms). In addition, the size of the cavity after bridge connection can be controlled in order to recognize specific ions. This is a very good choice to recognize sensors of different ions.

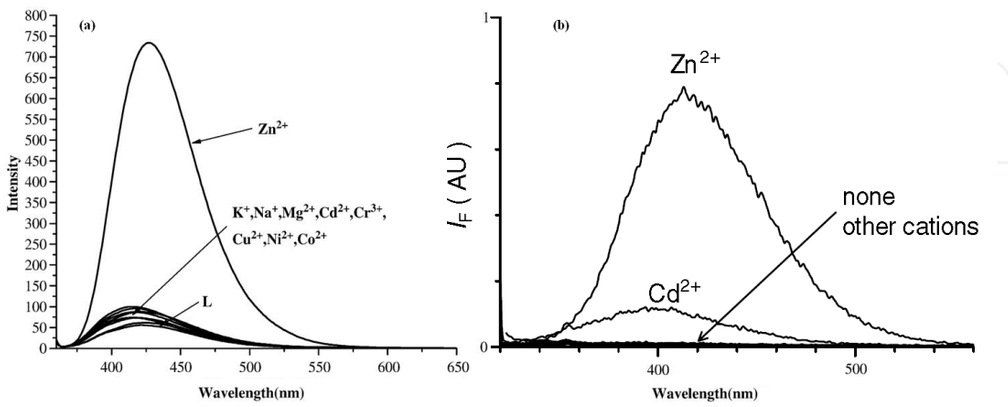


Fig. 8. (a) Fluorescence intensity of 12 (10 μM) in the presence of various metal ions (20 μM) in acetonitrile solution (λ_{ex}=305 nm, λ_{em}=423 nm). (b) Fluorescence spectra and intensity (monitored at 410 nm) of 13 (50 μ M) measured with respective metal cations (1 equiv) at pH 7.0 (KH_2PO_4–NaOH buffered solution).

Although quinoline based chemosensors can serve as both the metal ligand and the fluorophore, their optical properties limit the application in vivo. The main disadvantage of these chemosensors is high-energy UV excitation which is detrimental to cells. Fluorescence at short wavelengths (most of the emission wavelengh is under 500nm) and most of the fluorescent sensors, based on quinoline with DPA as receptor, are more or less affected by Cd^{2+}. So how to improve quinoline-based sensor is still a challenge.

5.2 Detection of Cd^{2+}

The interference of Cd^{2+} is a well-known problem for zinc fluorescence sensors and cadmium fluorescence sensors. Xue (2009) et al. reported an chemosensor that modulated the 8-position oxygen of the quinoline platform on sensor 14, while bound Zn^{2+} in 14 can be displaced by Cd^{2+}, resulting in another ratiometric sensing signal output (Fig. 9a). 14 shows a blue-shift of 33nm in emission spectrum. ^{1}H-NMR and optical spectra studies indicate that that 14 has higher affinity for Cd^{2+} than for Zn^{2+}, which consequently incurs the ion displacement process. Recently Xue (2011) et al., synthesized a new cadmium sensor 15 based on 4-isobutoxy-6-(dimethylamino)-8-methoxyquinaldine in line with the ICT mechanism. Sensor 15 exhibits very high sensitivity for Cd^{2+} (K_d=51pM) and excellent selectivity response for detection Cd^{2+} from other heavy and transition metal ions, such as Na^+, K^+, Mg^{2+}, and Ca^{2+} at millimolar level. They also established a single-excitation, dual-emission ratiometric measurement with a large blue shift in emission ($\Delta\lambda$ = 63 nm) and remarkable changes in the ratio (F_{495} nm/F_{558} nm) of the emission intensity (R/R_0 up to 15-fold, Fig. 9b). The crystal structures data of 15 binding with Cd^{2+} and Zn^{2+} demonstrate that the DPA moiety plays the main function of grasping the metal ions, while the 8-position

methoxy oxygen can be used to tune the selectivity of the sensor. Furthermore, confocal experiments in HEK 293 cells were carried out with 15, demonstrating 15 to be a ratiometric chemosensor to image intracellular, which is obviously superior to intensity-based images of the sole emission channel. This job is a guide to design Quinoline-based Cd^{2+} sensor.

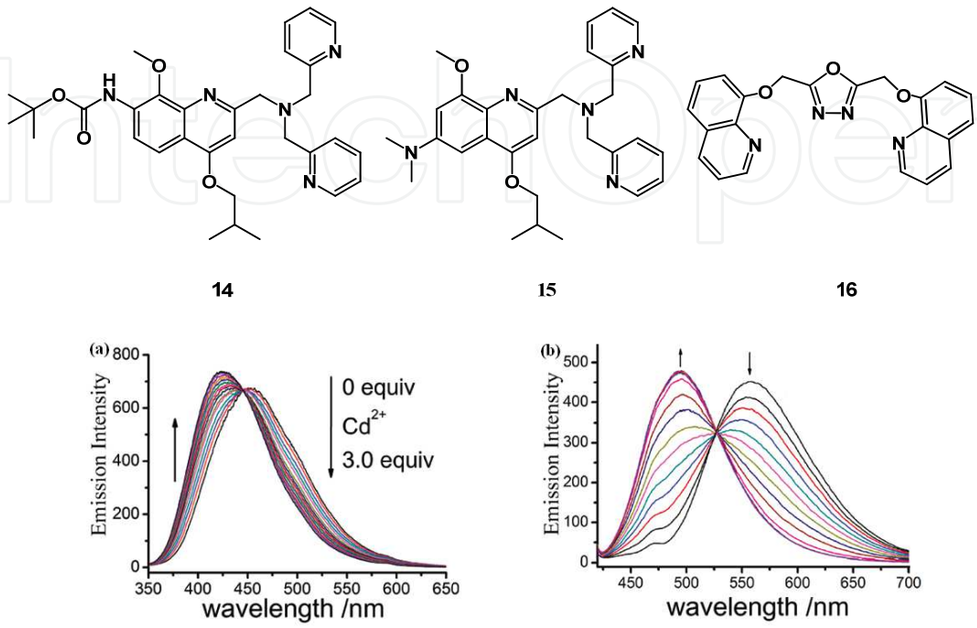


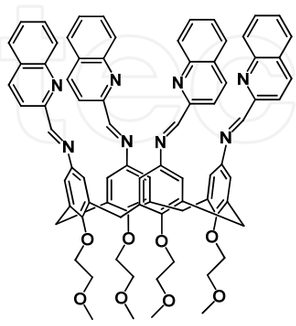
Fig. 9. (a) Fluorescence spectra (λ_{ex}=295 nm) of 10 μM 14 + 1 equiv of Zn^{2+} upon the titration of Cd^{2+} (0-3.0 equiv) in buffer solution. (b) Fluorescence spectra (λ_{ex} = 405 nm) of 10 μM 15 upon titration of Cd^{2+} (0-20 μM) in aqueous buffer.

Tang (2008) et al. merged 8-hydroxyquinoline with oxadiazole to develop a ratiometric chemosensor 16 for Cd^{2+}. If 1,3,4-oxadiazole subunit contained lone electron pairs on N, the semirigid ligand could effectively chelate Cd^{2+} according to the ionic radius and limit the geometric structure of the complex; thus 16 showed very high selectivity over other heavy and transition metal ions. This is also a designing method of bridge connection, that is, to make the detection group to form half heterocycle structure through the bridge, control the size of the heterocycle, and use the affinity of different heteroatoms to different ions, so that the selective recognition of different ions can be reached.

5.3 Detection of Cu^{2+} and Ag^{+}

Calixarenes are an important class of macrocyclic compounds, and they have been widely used as an ideal platform for the development of fluorescence chemosensors for alkali and alkaline-earth metal ions. Li (2008) et al. reported a turn on fluorescent sensor 17 for detecting Cu^{2+} based on calyx[4]arene bearing four iminoquinoline, which showed a largely enhanced fluorescent signal (1200-fold) upon addition of Cu^{2+} and a high selectivity toward Cu^{2+} over others. The 1:1 binding mode between sensor and Cu^{2+} was indicated by JOB's plot and mass spectrum. In Moriuchi-Kawakami's (2009) study, Cyclotriveratrylene can also act as a host analogous to calixarenes, a new C3-functionalized cyclotriveratrylene (CTV) bearing three fluorogenic quinolinyl groups. Sesnor 18 was synthesized, meanwhile, the

fluorescence emission was remarkably increased by the addition of Cu2+ with 1332% efficiency. In the two operations, the main function of quinoline is reflected in fluorescence changes before and after its N atom coordination. With regard to the selectivity of ions, it is decided by the cavity size formed by the middle cyclocompounds. The design is instructional, because compared with the bridge mentioned before, it produces a three-dimensional bridge, and brings about better selectivity of particular ions.



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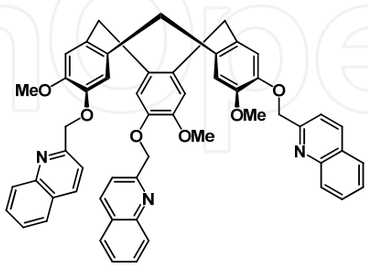
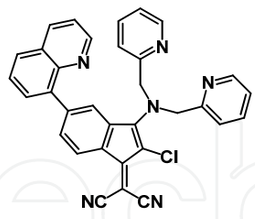


18

Although quinoline moiety can be used both as the metal binding site and the fluorophore, the application of quinoline-based chemosensors in biological systems is limited by their optical properties. The main disadvantage of these chemosensors is high-energy UV excitation, which is possibly detrimental to biological tissues. It can induce autofluorescence from endogenous components and fluorescence at short wavelengths. Chemosensors 19 developed by Ballesteros (2009) et al. enlarged the conjugated system with 5-bromoindanone at the 8-position by Suzuki reaction. With this improvement, after being excited by visible light (λ_{ex}=495nm), 19 showed a 5-fold increase in the intensity of emission centered at 650 nm after Cu^{2+} was added.



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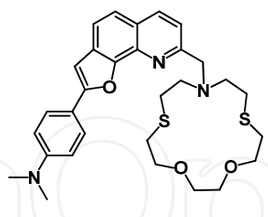

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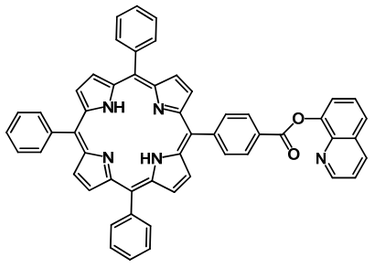
Receptor is a key role in the design of chemosensors, by choosing azacrown[N,S,O] instead of DPA. Wang (2010) et al. synthesized a new chemosensor 20 based on ICT mechanism. Chemosensor 20 is an effective ratiometric fluorescent sensor for silver ion and bears the features of a large Stokes shift at about 173 nm, with red-shift up to 50 nm in the emission spectra, and brings high affinity for silver ions (log K = 7.21) in ethanol in comparison with other competitive d^{10} metal ions. Crown compounds are all along used as highly recognized receptor groups for particular ions. As for groups which are not easily bounded, for instance, K^+, 18-crown-6 can be used to recognize it. However, crown compounds have some application limits. At the beginning, crown compounds comprised of different heteoatoms can not achieve highly efficient synthesis. Then, they are considerably

poisonous to in vivo cells. This imposes restrictions on their application in organisms to some extent.

5.4 Detection of Hg^{2+}

Modified quinoline can also become very good binding group for Hg^{2+} ion. Han (2009) et al. reported highly selective and highly sensitive Hg^{2+} chemosensor 21 based on quinoline and porphyrin ring. The 21 complexation quenches the fluorescence of porphyrin at 646 nm and induces a new fluorescent enhancement at 603 nm. The fluorescent response of 21 towards Hg^{2+} and ^{1}H-NMR indicates Hg^{2+} ion is binding with the quinoline moiety. Yang (2007) et al. reported chemosensor 22, which connect 8-hydroxyquinoline with rhodamine and ferrocene, and recognize Hg^{2+} through opening and closing rhodamine ring before and after binding. At the same time, because the density of the interior electron cloud changes before and after binding, the electrochemistry signal of ferrocene varies, so that the detection accuracy is improved. Concerning Hg^{2+} recognition, there is another method that receives considerable attention, that is, modified thioamides on quinoline, using the sulfur addicting feature of Hg^{2+}, will be transformed into amides by Hg^{2+}, which will change the PET process, thus inducing the production of fluorescence.



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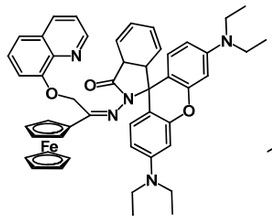

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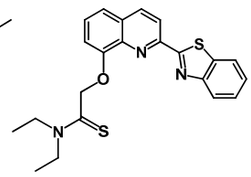


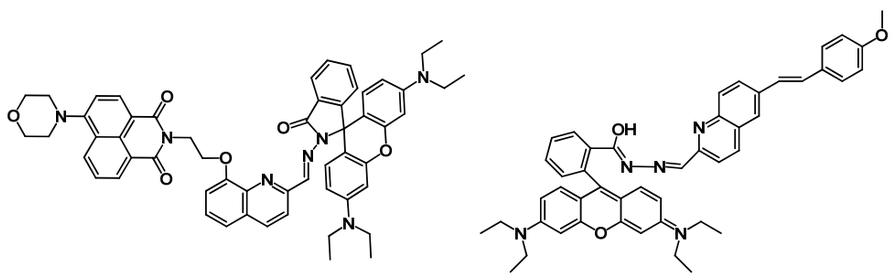
23

Song (2006) et al. reported 8-hydroxyquinoline derivative chemosensor 23. In 23, the fluorescence background is very weak. 23 is demonstrated to be highly sensitive to the detection of Hg^{2+}, because the hydrolytic conversion of thioamides into amides catalyzed by Hg^{2+} is very efficient. NMR, IR, and mass studies indicate the Hg^{2+} ion induced the transformation of thioamide into amide.

5.5 Detection of Cr^{3+} and Fe^{3+}

Because paramagnetic Fe^{3+} and Cr^{3+} are reported as two of the most efficient fluorescence quenchers among the transition metal ions, the development of Fluorescence chemosensors working with these inherent quenching metal ions is a challenging job. Zhou (2008) et al. reported a FRET-based Cr^{3+} chemosensor 24. With increased FRET from 1,8-naphthalimide (donor) to the open, colored form of rhodamine (acceptor), the intensity of the fluorescent peak at 544 nm gradually decreased and that of new fluorescent band centered at 592 nm increased, 24 showed an 7.6-fold increase in the ratio of emission intensities (F_{592} nm/F_{544} nm). We (2011) reported a turn-on fluorescent probe 25 for Fe^{3+} based on the rhodamine platform. An improved quinoline fluorescent group, which could be excited by about 400 nm wavelength of light, was linked to the rhodamine platform. The emission of conjugated

quinoline was partly in the range of rhodamine absorption, so 1,8-naphthalimide could be removed. And we also removed the hydroxy group at 8-position to reach a different coordination mode choice on the Fe^{3+} ions. 25 shows high selectively for Fe^{3+} over Cr^{3+} both in fluorescence and visible light (Fig. 10). JOB's plot indicate that, the 1:2 binding model between Fe^{3+} and 25, pH and cytotoxic effect also suggest that the new sensor is suitable for bioimaging. More importantly, the improved quinoline group can be excited by 800nm two-photon laser source, which is more suitable for bioimaging. We can utilize the FRET processes of quinoline and other fluorescent groups to design sensors, so as to take advantage of their respective merits. For example, we can make use of other groups' visible light changes, water solubility, and high sensitivity brought about by switch construction and so on to compensate demerits of quinoline groups. This will be one of the directions for designing sensors.



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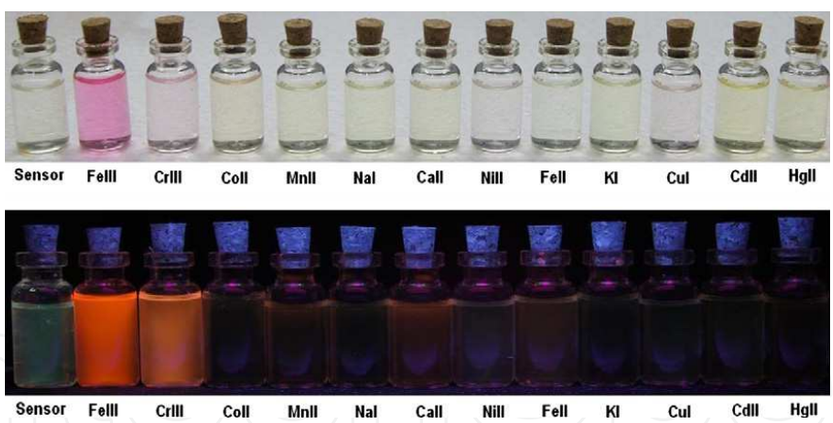

Fig. 10. Top: color of 25 and 25 with different metal ions. Bottom: fluorescence (λ_{ex} = 365 nm) change upon addition of different metal ions.

6. Conclusion

In this review, we cover quinoline-based chemosensors for detection of different metal ions. There has been tremendous interest in improving quinoline-based chemosensors due to its easy synthesis method, high sensitivity and stability. However, there is still much room for progress in its application in vivo such as water solubility, high selectivity, and fluorescence bio-imaging capacity. Accordingly, the design of receptor for different ions is very important. For example, 15 adopted the different bonding model to distinguish between

Zn^{2+} and Cd^{2+}. 24, through another fluorophore, thus achieved FRET process. Extended conjugated system of quinoline can be excited by two-photon laser source, and so on. We anticipate that more and more quinoline-based fluorescence chemosensors can be synthesized which are useful for detection of metal ions.

7. Acknowledgements

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8. References

Aoki, S.; Sakurama, K.; Matsuo, N.; Yamada, Y.; Takasawa, R.; Tanuma, S.; Shiro, M.; Takeda, K. & Kimura, E. (2006). A New Fluorescent Probe for Zinc(II): An 8-Hydroxy -5-N,Ndimethylaminosulfonylquinoline-Pendant 1,4,7,10-Tetraazacyclododecane. *Chemistry –A European journal* 12, 9066-9080

Ballesteros, E.; Moreno, D.; Gomez, T.; Rodriguez, T.; Rojo, J.; Garcia-Valverde, M. & Torroba, T. (2009). A New Selective Chromogenic and Turn-On Fluorogenic Probe for Copper(II) in Water-Acetonitrile 1:1 Solution. *Organic Letters* 11, 1269-1272

Banthia, S. & Samanta, A. (2006). A New Strategy for Ratiometric Fluorescence Detection of Transition Metal Ions. *The Journal of Physical Chemistry B* 110, 6437-6440

Bhalla, V.; Tejpal, R.; Kumar, M. & Sethi, A. (2009). Terphenyl Derivatives as "Turn On" Fluorescent Sensors for Mercury. *Inorganic Chemistry* 48, 11677-11684

Burdette, A. C. & Lippard, S. J. (2003). A Selective Turn-On Fluorescent Sensor for Imaging Copper in Living Cells. *Proceeding of the national academy of Science of the United States of America* 100, 3605-3610

Chen, X. –Y.; Shi, J.; Li, Y. –M.; Wang, F. –L.; Wu, X.; Guo, Q. –X. & Liu, L. (2009). Two-Photon Fluorescent Probes of Biological Zn(II) Derived from 7-Hydroxyquinoline. *Organic Letters* 11, 4426-4429

de Silva, A. P.; Nimal Gunaratne, H. Q.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T. & Rice, T. E. (1997). Fluorescence-Based Sensing of Divalent Zinc in Biological Systems. *Chemical Reviews* 97, 1515-1566

Dobson, S. (1992) Cadmium: EnVironmental Aspects; World Health Organization:Geneva. ISBN 92-4-157135-7

Doebner, O.; Von Miller, W. & Ber, D. T. (1996). Synthesis of Pyrroloquinolinequinone Analogs Molecular Structure and Moessbauer and Magnetic Properties of Their Iron Complexessch. *Chem. Ges* 34, 6552-6555

Dujols, V.; Ford, F. & Czarnik, A. W. (1997). A Long-Wavelength Fluorescent Chemodosimeter Selective for Cu(II) Ion in Water. *Journal of American Chemistry Society* 119, 7386-7387

Falchuk, K. H. (1998). The molecular basis for the role of zinc in developmental biology. *Molecular and Cellular Biochemistry* 188, 41-48

Frederickson, C. J.; Kasarskis, E. J.; Ringo, D. & Frederickson, R. E. (1987). A quinoline fluorescence method for visualizing and assaying the histochemically reactive zinc (bouton zinc) in the brain. *Journal of Neuroscience Methods* 20, 91-103

Guerrini, G.; Taddei, M. & Ponticelli, F. (2011). Synthesis of Functionalized Quinolines and Benzo[c][2,7]naphthyridines Based on a Photo-Fries Rearrangement. *The Journal of Organic Chemistry* 76, 7597-7601

Han, Z. –X.; Luo, H. –Y.; Zhang, X. –B.; Kong, R. –M.; Shen, G. –L. & Yu, R. –Q. (2009). A ratiometric chemosensor for fluorescent determination of Hg2+ based on a new porphyrin-quinoline dyad. Spectrochimica Acta Part A: *Molecular and Biomolecular Spectroscopy* 72, 1084-1088

Hanaoka, K.; Kikuchi, K.; Kojima, H.; Urano, Y. & Nagano, T. (2004). Development of a Zinc Ion-Selective Luminescent Lanthanide Chemosensor for Biological Applications. *Journal of the American Chemical Society* 126, 12470-12476

Henary, M. M.; Wu, Y. & Fahrni, C. J. (2004). Zinc(II)-Selective Ratiometric Fluorescent Sensors Based on Inhibition of Excited-State Intramolecular Proton Transfer. *Chemistry –A European Journal* 10, 3015-3025

Hirano, T.; Kikuchi, K.; Urano, Y. & Nagano, T. (2002). Improvement and Biological Applications of Fluorescent Probes for Zinc, ZnAFs. *Journal of the American Chemical Society* 124, 6555-6562

Joshi, B. P.; Lohani, C. R. & Lee, K. H. (2010). A highly sensitive and selective detection of Hg(II) in 100% aqueous solution with fluorescent labeled dimerized Cys residues. *Organic & Biomolecular Chemistry* 8, 3220-3226

Jung, H. S.; Ko, K. C.; Lee, J. H.; Kim, S. H.; Bhuniya, S.; Lee J. Y.; Kim, Y.; Kim, S. J. & Kim, J. S. (2010). Rationally designed fluorescence turn-on sensors: a new design strategy based on orbital control. *Inorganic Chemistry* 49, 8552-8557

Komatsu, K.; Urano, Y.; Kojima, H. & Nagano, T. (2007). Development of an Iminocoumarin-Based Zinc Sensor Suitable for Ratiometric Fluorescence Imaging of Neuronal Zinc. *Journal of the American Chemical Society* 129, 13447-13454

Kimber, M. C.; Mahadevan, I. B.; Lincoln, S. F.; Ward, A. D. & Tiekink, E. R. T. (2000). The Synthesis and Fluorescent Properties of Analogues of the Zinc (II) Specific Fluorophore Zinquin Ester. *Journal of Organic Chemistry* 65, 8204-8209

Lee, D. Y.; Singh, N.; Kim, M. J. & Jang, D. O. (2010). Ratiometric fluorescent determination of Zn(II): a new class of tripodal receptor using mixed imine and amide linkages. *Tetrahedron* 66, 7965-7969

Li, G. –K.; Xu, Z. –X.; Chen, C. –F. & Huang, Z. –T. (2008). A highly efficient and selective turn-on fluorescent sensor for Cu2+ ion based on calix[4]arene bearing four iminoquinoline subunits on the upper rimw. *Chemical Communications* 1774-1776

Lim, N. C.; Schuster, J. V.; Porto, M. C.; Tanudra, M. A.; Yao, L.; Freake, H. C. & Brûckner, C. (2005). Coumarin-Based Chemosensors for Zinc(II): Toward the Determination of the Design Algorithm for CHEF-Type and Ratiometric Probes. *Inorganic Chemistry* 44, 2018-2030

Liu, Z. –C.; Wang, B. –D.; Yang, Z. –Y.; Li, T. –R. & Li, Y. (2010). A novel fluorescent chemosensor for Zn(II) based on 1,2-(2′-oxoquinoline-3′-yl-methylideneimino) ethane. *Inorganic Chemistry Communications* 13, 606-608

Marct, W.; Jacob, C.; Vallee, B. L. & Fishcher, E. H. (1999). Inhibitory sites in enzymes: zinc removal and reactivation by thionein. *Proceeding of the national academy of Science of the United States of America* 96, 1936-1940

Mason, W. T. (1999). Fluorescent and Luminescent Probes for Biological Activit., 2nd cd.; Academic Press: New York. ISBN 0-12-447836-0

Anthea, M.; Hopkins, J.; McLaughlin, C. W.; Johnson, S.; Warner, M. Q.; LaHart, D. & Wright J. D. (1993). Human Biology and Health. Englewood Cliffs, New Jersey, USA: Prentice Hall. ISBN 0-13-981176-1

Matsubara, Y.; Hirakawa, S.; Yamaguchi, Y. & Yoshida, Z. (2011). Assembly of Substituted 2-Alkylquinolines by a Sequential Palladium-Catalyzed C-N and C-C Bond Formation). *Angew Angewandte Chemie International Edition* 50, 7670-7673

Meng, X. M.; Zhu, M. Z.; Liu, L. & Guo, Q. X. (2006). Novel highly selective fluorescent chemosensors for Zn(II). *Tetrahedron Letters* 47, 1559-1562

Mizukami, S.; Okada, S. & Kimura, S. (2009). Design and Synthesis of Coumarin-based Zn2+ Probes for Ratiometric Fluorescence Imaging. *Inorganic Chemistry* 48, 7630-7638

Moriuchi-Kawakami, T.; Sato, J. & Shibutani, Y. (2009). C3-Functionalized Cyclotriveratrylene Derivative Bearing Quinolinyl Group as a Fluorescent Probe for Cu2+. *Analytical Sciences* 25, 449-452

Nolan, E. M.; Jaworski, J.; Okamoto, K. -I.; Hayashi, Y.; Sheng, M. & Lippard, S. J. (2005). QZ1 and QZ2: Rapid, Reversible Quinoline-Derivatized Fluoresceins for Sensing Biological Zn(II). *Journal of the American Chemical Society* 127, 16812-16823

Pearce, D. A.; Jotterand, N.; Carrico, I. S. & Imperiali, B. (2001). Derivatives of 8-Hydroxy-2-methylquinoline are Powerful Prototypes for Zinc Sensors in Biological Systems. *Journal of the American Chemical Society* 123, 5160-5161

Peng, X. J.; Du, J. J.; Fan, J. L.; Wang, J. Y.; Wu, Y. K.; Zhao, J. Z.; Sun, S. G. & Xu, T. (2007). A Selective Fluorescent Sensor for Imaging Cd2+ in Living Cells. *Journal of American Chemistry Society* 129, 1500-1501

Sarkar, M.; Banthia, S.; Patil, A.; Ansari, M. B. & Samanta, A. (2006). pH-Regulated ''Off–On'' fluorescence signalling of d-block metal ions in aqueous media and realization of molecular IMP logic function. *New Jornal of Chemistry* 30, 1557-1560

Sarkar, M.; Banthia, S. & Samanta, A. (2006). A highly selective 'off–on' fluorescence chemosensor for Cr(III). *Tetrahedron Letters* 47, 7575-7578

Shiraishi, Y.; Ichimura, C. & Hirai, T. (2007). A quinoline–polyamine conjugate as a fluorescent chemosensor for quantitative detection of Zn(II) in water. *Tetrahedron Letters* 48, 7769-7773

Shults, M. D.; Pearce, D. A. & Imperiali, B. (2003). Versatile Fluorescence Probes of Protein Kinase Activity. *Journal of the American Chemical Society* 125, 14248-14249

Song, K. C.; Kim, J. S.; Park S. M.; Chung, K. –C.; Ahn, S. & Chang, S. –K. (2006). Fluorogenic Hg2+-Selective Chemodosimeter Derived from 8-Hydroxyquinoline. *Organic Letters* 8, 3413-3416

Tang, X. –L.; Peng, X. –H.; Dou, W.; Mao, J.; Zheng, J. –R.; Qin, W. –W.; Liu, W. –S.; Chang, J. & Yao, X. –J. (2008). Design of a Semirigid Molecule as a Selective Fluorescent Chemosensor for Recognition of Cd(II). *Organic Letters* 10, 3653-3656

Teolato, P.; Rampazzo, E.; Arduini, M.; Mancin, F.; Tecilla, P. & Tonellato, U. (2007). Silica Nanoparticles for Fluorescence Sensing of ZnII:Exploring the Covalent Strategy. *Chemistry –A European journal* 13, 2238-2245

Vallee, B. L. & Falchuk, K. H. (1993). The biochemical basis of zinc physiology. *Physiological Reviews* 73, 79-118

van Dongen, E. M. W. M.; Dekkers, L. M.; Spijker, K.; Meijer, E. W.; Klomp, L.W. W. J. & Merkx, M. (2006). Ratiometric Fluorescent Sensor Proteins with Subnanomolar

Affinity for Zn(II) Based on Copper Chaperone Domains. *Journal of the American Chemical Society* 128, 10754-10762

Walkup, G. K.; Burdette, S. C.; Lippard, S. J. & Tsien, R. Y. (2000). A New Cell-Permeable Fluorescent Probe for Zn2+. *Journal of the American Chemical Society* 122, 5644-5645

Wang, H. –H.; Xue, L.; Qian, Y. –Y. & Jiang, H. (2010). Novel Ratiometric Fluorescent Sensorfor Silver Ions. *Organic Letters* 12, 292-295

Wang, S. X.; Meng, X. M. & Zhu, M. Z. (2011). A naked-eye rhodamine-based fluorescent probe for Fe(III) and its application in living cells. *Tetrahedron Letters* 52, 2840-2843

Wang, X. H.; Cao, J. & Chen, C. F. (2010). A Highly Efficient and Selective Turn-on Fluorescent Sensor for Cu2+ Ion. *Chinese Journal of Chemistry* 28, 1777-1779

Wolf, C.; Mei, X. F. & Rokadia, H. K. (2004), Selective detection of Fe(III) ions in aqueous solution with a 1,8-diacridylnaphthalene-derived fluorosensor. *Tetrahedron Letters* 45, 7867-7871

Woodroofe, C. C.; Masalha, R.; Barnes, K. R.; Frederickson, C. J. & Lippard, S. J. (2004). Membrane-Permeable and -Impermeable Sensors of the Zinpyr Family and Their Application to Imaging of Hippocampal Zinc In Vivo. *Chemistry & Biology* 11, 1659-1666

Woodroofe, C. C. & Lippard, S. J. (2003). A Novel Two-Fluorophore Approach to Ratiometric Sensing of Zn2+. *Journal of the American Chemical Society* 125, 11458-11459

Xue, L.; Wang, H. –H.; Wang, X. –J. & Jiang, H. (2008). Modulating Affinities of Di-2-picolylamine (DPA)-Substituted Quinoline Sensors for Zinc Ions by Varying Pendant Ligands. *Inorganic Chemistry* 47, 4310-4318

Xue, L.; Liu, C. & Jiang, H. (2009). A ratiometric fluorescent sensor with a large Stokes shift for imaging zinc ions in living cellsw. *Chemical Communications* 1061-1063

Xue, L.; Liu ,Q. & Jiang, H. (2009). Ratiometric Zn2+ Fluorescent Sensor and New Approach for Sensing Cd2+ by Ratiometric Displacement. *Organic Letters* 11, 3454-3457

Xue, L.; Li, G. P.; Liu, Q.; Wang, H. H.; Liu, C.; Ding, X.; He, S. & Jiang, H. (2011). Ratiometric Fluorescent Sensor Based on Inhibition of Resonance for Detection of Cadmium in Aqueous Solution and Living Cells. *Inorganic Chemistry* 50, 3680-3690

Yang, H.; Zhou, Z.; Huang, K.; Yu, M.; Li, F.; Yi, T. & Huang, C. (2007). Multisignaling Optical-Electrochemical Sensor for Hg2+ Based on a Rhodamine Derivative with a Ferrocene Unit. *Organic Letters* 9, 4729-4732

Zalewski, P. D.; Forbes, I. J. & Betts, W. H. (1993). Correlation of apoptosis with change in intracellular labile Zn(II) using zinquin [(2-methyl-8-p-toluenesulphonamido-6-quinolyloxy)acetic acid], a new specific fluorescent probe for Zn(II). *Biochemical Journal* 296, 403-408

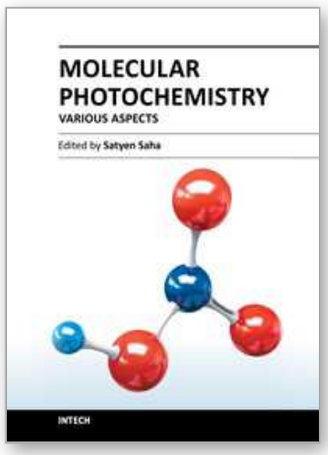
Zalewski, P. D.; Forbes, I. J.; Borlinghaus, R.; Betts, W. H.; Lincoln, S. F. & Ward, A. D. (1994). Flux of intracellular labile zinc during apoptosis (gene-directed cell death) revealed by a specific chemical probe, Zinquin. *Chemistry & Biology* 1, 153-161

Zalewski, P. D.; Millard, S. H.; Forbes, I. J.; Kapaniris, O.; Slavotinek, A.; Betts, W. H.; Ward, A. D.; Lincoln S. F. & Mahadevan, I. (1994). Video image analysis of labilc zinc in viable pancreatic islet cells using a specific fluorescent probe for zinc. *Journal of Histochemistry and Cytochemistry* 42, 877-884

Zhang, Y.; Guo, X. F.; Si, W. X.; Jia, L. & Qian, X. H. (2008). Ratiometric and Water-Soluble Fluorescent Zinc Sensor of Carboxamidoquinoline with an Alkoxyethylamino Chain as Receptor. *Organic Letters* 10, 473-476

Zhou, X. Y.; Yu, B. R.; Guo, Y. L.; Tang, X. L.; Zhang, H. H. & Liu, W. S. (2010). Both Visual and Fluorescent Sensor for Zn2+ Based on Quinoline Platform. *Inorganic Chemistry* 49, 4002-4007

Zhou, Z.; Yu, M.; Yang, H.; Huang, K.; Li, F.; Yi, T. & Huang C. (2008). FRET-based sensor for imaging chromium(III) in living cellsw. *Chemical Communications* 3387-389



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There have been various comprehensive and stand-alone text books on the introduction to Molecular Photochemistry which provide crystal clear concepts on fundamental issues. This book entitled "Molecular Photochemistry - Various Aspects" presents various advanced topics that inherently utilizes those core concepts/techniques to various advanced fields of photochemistry and are generally not available. The purpose of publication of this book is actually an effort to bring many such important topics clubbed together. The goal of this book is to familiarize both research scholars and post graduate students with recent advancement in various fields related to Photochemistry. The book is broadly divided in five parts: the photochemistry I) in solution, II) of metal oxides, III) in biology, IV) the computational aspects and V) applications. Each part provides unique aspect of photochemistry. These exciting chapters clearly indicate that the future of photochemistry like in any other burgeoning field is more exciting than the past.

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